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STUDIES IN BERIBERI.

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INTRODUCTION.

The investigation of the many unsolved problems in beriberi, both in regard to the character and the special and general features of the disease, presents many profound difficulties. Almost all modern writers have called attention to this fact. For instance, Wright,[1] in the introduction to his recent monograph on beriberi, says:

> Probably there is no disease whose etiology is so much a matter of speculation as that of beriberi. Certainly there is no disease whose literature when read leaves one in so great a state of mental confusion. Nitrogen starvation, pernicious anæmia, infected fish and raw fish diet, arsenical, carbon dioxide, and miasmatic intoxication, bacterial and plasmodial infection are amongst the many direct causes put forward to account for it. They are largely speculative or founded on superficial or one-sided observation. No one of them is generally accepted. Many of them may and ought to be excluded as chief pathogenic factors.

Durham,[2] who succeeded Wright as an investigator of beriberi in the Malay Peninsula, and who came to conclusions materially differing from those of his predecessor, likewise emphasizes the great difficulties encountered in the study of this disease, and writes as follows:

> The literature of beriberi is so great and at the same time so divergent, and so contradictory are the views and records that have been given, that I have

[1] Wright: An Inquiry into the Etiology and Pathology of Beriberi. *Publications of the Federated Malay States*, Singapore (1902), May.

[2] Durham, Herbert E.: Notes on Berberi in the Malay Peninsula and on Christmas Island. *Journal of Hygiene* (1904), 4, 112.

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excluded it as far as possible from these notes. When the day of complete knowledge of the nature of beriberi shall arrive, it must assuredly happen that many of the hitherto published records will disappear, from their failure to mention the circumstances which attend the real cause.

The present writer, after having investigated a number of cases of beriberi both from a clinical and pathological standpoint, occurring in Manila between February, 1904, and August, 1905, was directed during the latter month to proceed to Japan for the purpose of studying the large amount of *kakke* material which had accumulated in the military hospitals of Hiroshima and Tokyo during the late Russo-Japanese war. A brief preliminary report concerning these studies has already been published in this journal.[3] In the discussion which follows it is the intention to present to the practitioner who may be called upon to diagnosticate and to treat cases of beriberi, a systematic general outline of the affection, and at the same time there has been included an account of the investigations which have been carried on with the view of finding the specific micro-organism which causes this disease and of confirming or denying the recent claim of Okata and Kokubo concerning the discovery of the causative factor of the malady. A detailed summary of the first Japanese publication on the Okata-Kokubo kakke coccus was given in my preliminary report. These Japanese army surgeons have published a number of further contributions since this publication appeared and have reaffirmed their statements as to the specific nature of their coccus. However, we can not confirm their claims, since we find that this organism certainly is not the etiological factor in beriberi. In fact, none of the bacteria and other micro-organisms from time to time proposed as being the cause of this mysterious disease can be considered to be specific. I have not, for obvious reasons, given a lengthy review of the literature of beriberi. The greater part of it to-day is merely of historical interest.

DEFINITION.

Beriberi—*Polyneuritis endemica* (Baelz), *Neuritis multiplex endemica* (Scheube)—may be defined as an acute, subacute, or chronic infectious disease, characterized clinically by disturbances of the circulation, of motion and of sensation, and associated anatomically with hypertrophy and degeneration of the heart, of the peripheral nerves, and of the voluntary muscles.[4]

[3] Herzog: Beriberi in the Japanese Army During the Late War. *Phil. Journ. Science*, February (1906), 1, 169.

[4] A complete discussion of the nomenclature is given in Scheube's *Die Krankheiten der warmen Länder* (1903), Jena, and *Die Beriberi-Krankheit* (1894), Jena. These two publications of Scheube include a summary of the literature of beriberi up to 1903, comprising about 700 books, monographs, and other articles.

HISTORY AND GEOGRAPHICAL DISTRIBUTION.

The first undoubted mention of beriberi is made in a Chinese work of the second century of the Christian era, and a good description of the disease is to be found in a Chinese text-book on medicine of the sixth century. It is also possible that the disease may very early have appeared in the Western Hemisphere, because two quotations from Strabo and Dio Cassius, giving a description of a Roman invasion of Arabia in the year 24 B. C., perhaps refer to an epidemic of beriberi among the soldiers of the Roman army.

The disease is now generally prevalent in tropical and subtropical regions in which as a rule the humidity is considerable. It is found in Asia, Japan (including Formosa), China, the Malay Archipelago and Peninsula, the Dutch Possessions, and in Eastern India. It occurs on the eastern coast of South America, particularly in Brazil, and a number of reports of its presence in Africa during the last two decades have appeared.[5] Some isolated epidemics have also taken place in England and Ireland, and sporadic, imported cases have been encountered in Continental Europe, the United States, and Canada. It is also prevalent among the native population throughout the Philippine Islands. During the early days of the American occupation of Manila a few cases occurred among the white troops, but for several years beriberi has certainly been of very rare occurrence among the Americans, the author having only seen two cases during two years. One was in a teacher who had returned to Manila from Mindanao, the other in a physician who for several years had been in charge of the Mindoro prison, which formerly was one of the most notorious foci of beriberi in the Islands, but which was abandoned some time ago.

THE FIRST EPIDEMIC OF BERIBERI IN THE PHILIPPINE ISLANDS.

It is somewhat strange that the records concerning beriberi in these Islands date back only a few decades. Königer[6] in 1884 reported what he considers the first invasion of the Philippines by beriberi, the epidemic occurring during the year 1882–1883. In view of the fact that the disease has for many centuries been so widespread in Japan, it is hardly credible that the Philippines should have been exempt from it until 1882. Moreover, it is an historical fact that during the constant feudal strife and the civil wars preceding the establishment of the Fogugawa Shogunate many impoverished Japanese frequently were forcibly exported to the Philippine Islands by Portuguese slave traders and sold as slaves. Besides, northern Luzon was once invaded by a Japanese army.[7] It is generally claimed in the Philippine Islands that leprosy

[5] According to A. Plehn it has been observed in the latter country in the following places: Reunion, Mauritius, Nossi-be, Zanzibar, Cope Colony, Senegal, Angola, Congo State, German West Africa (Kamerun).

[6] Königer: Ueber epidemisches Auftreten von Beriberi in Manila, 1882–1883. *Deutsch. Archiv. für Klin. Medizin* (1884), **35**, 419.

[7] Griffis: *The Mikado's Empire*, 9th edition, New York (1900), 246 and 254.

was brought to the Archipelago from Japan, and under these circumstances it would be remarkable if beriberi had not been imported into Manila before the date given by Königer. However, the latter author has given us a very interesting report of what he considered to be the first invasion of the Philippine Islands by the disease. His article may be briefly summarized as follows:

"From August to October, 1882, Manila was visited by a severe cholera epidemic, which there found a fertile soil and carried off between 15,000 and 20,000 victims (the population of Manila was estimated at 400,000). A panic occurred among the native as well as among the European population, because cholera had not been present since 1865 and as the mortality was more than 75 per cent. After the epidemic had subsided, on October 20, a terrible typhoon visited the city and province and destroyed all the suburban houses built of light material. As a consequence, almost the whole native population of Manila and its surroundings was without shelter. In Manila alone, 60,000 families had lost their homes. Nor was it possible rapidly to rebuild the destroyed houses and huts, since, following the typhoon, a flood occurred and all the lower parts of the city and province were under water for several weeks. Building material was scarce and very expensive. By this time, while the cholera epidemic was still smoldering, a new disease, which killed its victims in a few days or weeks, was noticed among the inhabitants. The native and Spanish physicians did not recognize the malady and the terror of the population increased. In some cases the disease was connected with a swelling of the glands and it therefore was believed by some to be a variety of bubonic plague. As soon as I saw the first cases, I had no doubt that I was dealing with a particularly malignant epidemic of beriberi, of which I had seen some cases in Japan. I caused a notice to be published by the Spanish medical board, explaining that the prevalent disease was not bubonic plague. The epidemic of beriberi rapidly spread in the province of Manila and along the coast to the neighboring territories. It remained stationary during November and December and gradually decreased during January. When I left Manila during the middle of March the epidemic had very much decreased, and there were also still present a number of sporadic cases of cholera."

"Beriberi had heretofore not been known in Manila. Whether the disease had occurred at all at this place during the last three centuries might perhaps be ascertained from a study of the friars' records. However, it was not known to the inhabitants, including the physicians, some of whom had practiced in Manila for more than forty years. I myself, during a practice of three years had never seen a case of beriberi. This first appearance of the disease in Manila is of particular interest because of the enormous mortality observed during the beginning of the epidemic. This mortality is not surpassed by anything heretofore reported and is higher than it is stated to be by almost all other observers. I have no reliable data as to the percentage of beriberi mortality during the first month. There are at present no official figures of value, and if subsequently any should appear they would not deserve any confidence. The general impression existing among physicians as well as laymen during the first part of the epidemic was that the disease was absolutely fatal. However, during the earlier part of the outbreak I saw several cases which recovered. Still, I think that a mortality of 60 per cent for the first month is by no means too high an estimate. As to the total number of deaths I have only one reliable observation, according to which during a period of a little more than two months, over 300 deaths from beriberi occurred in Malabon, a place of about 25,000 inhabitants, situated 7 kilometers from Manila. However, it is probable that this place suffered more

than any other in the vicinity. The conclusion certainly appears justified that the number of victims in the capital and the surrounding provinces reached several thousand."

Königer attributes the great mortality which he noticed in this epidemic of beriberi to the distress existing among the natives and to their very poor state of nutrition. Almost all of the cases were seen among the poorer classes, the author observing only two among Europeans, who, however, were also living under very unfavorable conditions. Among the Chinese the number was small as compared with that among the natives.

ETIOLOGY.

It is astonishing and at the same time embarrassing that the etiology of beriberi, a disease so widespread and one which has been the subject of such extensive investigations, is still but little understood, not merely as to its specific cause but also as to other concomitant factors favoring its appearance and spread. Manson,[8] in a recent article on this subject, expresses his views as follows:

"It is a somewhat humiliating fact that although beriberi is a disease of first-class importance in the Tropics, although it exhibits peculiarities in its epidemiology so striking that they seem to suggest that surely the cause can not be hard to find, and that although not a few investigators, medical and lay, have diligently set themselves to find this cause, they are about as ignorant of its true nature and of the medium in which it is applied and of the other etiologic circumstances as was Bontius when he wrote about beriberi over two hundred and fifty years ago. Quite recently there may have been some advances, but even these recent advances are more in the direction of showing what beriberi is not, rather than in the direction of showing what it is."

Scheube, to whom, as well as to Baelz, we owe so much of our knowledge concerning beriberi, believes that beriberi is an infectious disease and not a disturbance of the functions of nutrition caused by rice, fish, or insufficient nutrition. He points out that frequently strong, well-nourished young people suffer from beriberi, that the disease occurs independently of nutrition and other conditions of environment in certain well-defined districts, and that it is particularly prevalent at the seashore and along the banks of large rivers. He believes that the disease is not contagious, but that it may be and is carried along the lines of traffic by railroads and by vessels. He calls attention to the fact of the frequency of beriberi in places where human beings are crowded together, such as in prisons, schools, and factories. He also states that observations have been made in Japan showing clearly that the importation of a few cases of beriberi into a heretofore non-infected district has been followed by larger outbreaks of the disease, a fact which also has been reported by Robert Koch with reference to the introduction of the disease into New Guinea by some laborers coming from a distance. Scheube believes that beriberi is due to a micro-organism, either of a vegetable or of an animal nature, forming a toxin which acts upon the nervous system. He emphasizes the fact that beriberi shows a predilection for certain races, being very common among the Japanese, Chinese, and Malays and rare among the Europeans

[8] Manson: The Phophylaxis and Treatment of Beriberi. *Brit. Med. Journ.* (1902), 2, 830.

and Americans living in the East. It is more common among males than among females and it generally attacks individuals under 30 years of age.

Manson's theory as to the origin of beriberi is that the disease is a neuritis caused by a toxin, the latter being the product of a germ operating in some culture medium located outside of the human body. He believes that this toxin does not enter the body in food or in water but is inhaled or introduced through the skin.

Takagi, late surgeon-general of the Japanese navy, still adheres to the theory that *kakke* is due to an insufficient diet, particularly to one containing a large amount of rice. When he first studied the question of the etiology of beriberi, the ratio of beriberi patients in the Japanese naval force in 1883 was 231 per thousand. After the diet was changed, the number of *kakke* patients in this branch of the Japanese service diminished, so that in 1898 the ratio was only 0.87 per thousand. However, it has frequently been pointed out that during this period of time the number of *kakke* patients in Japan had also greatly diminished in districts and among bodies of men where such a radical change of diet had not taken place.

Experiments on several hundred prisoners in the Malay Peninsula during a period of eleven months furnished conclusive proof to Wright that beriberi was contracted, even though the diet was qualitatively and quantitatively correct. He thinks that his experiments positively eliminate diet, as such, as a factor in the causation of the disease.

Durham was struck by the fact that the well-to-do in and about the Federated Malay States escaped the disease, whereas people who were in poor surroundings were stricken, so that it was difficult not to believe that some food constituent, when sufficient in amount, protected the nervous system. However, he also noticed that beriberi may spread through a community in which the inhabitants are taking a sufficiently nitrogenous diet, and in proof of this he cites the instance of the prisoners in the gaol of the Federated Malay States. In spite of all, he thinks it is difficult, if not impossible, not to believe that the character of the food and the occurrence of beriberi are in some way related. Many of the published records seem to indicate such a connection, although the records of the Puda gaol show that the old theory of nitrogen starvation can not be upheld.

Stanley (l. c.) remarks that in Shanghai, China, beriberi as a rule becomes prevalent toward the end of the summer. He saw 500 cases among the Chinese prisoners in the municipal gaol and in three police stations from 1898 until 1902. Most of these occurred among the long-term prisoners, in spite of the fact that they lived under better conditions as regards ventilation, cleanliness, exercise, and food than they did prior to their incarceration. Beriberi among the better classes of the general population is rare in Shanghai. Stanley declares that he is unable to answer the question why beriberi should be so much more prevalent among the municipal prisoners than it is among the general Chinese population of the city.

Sambon [9] thinks that an enormous amount of evidence has been brought forward against the belief that rice diet is a direct causative factor in beriberi; however, this diet may be related to beriberi just as we now understand the consumption of maize to be related to pellagra; but nevertheless, he believes that the specific agent of beriberi lives within the patient's body. He finds the prevalence of the disease to be increased by a high temperature and an abundant rainfall, and recalls that it is chiefly an affection of the common laborer, that we are absolutely ignorant of the manner in which it is carried from place to place,

[9] Sambon: A Discussion on Beriberi. *Brit. Med. Journ.* (1902), 2, 835.

and that, whatever might be the cause of the malady, we can not deny that diet seems to have a potent influence on its frequency.

Two Japanese investigators, Ternuchi and Saiki,[10] have carried on some chemical investigations on a beriberi case which showed œdema, paralysis, hypæsthesia and other disturbances of motion and sensation. They found no interference with the digestion and absortion of nitrogenous food, but demonstrated that the nitrogen excretion in the urine was much increased, the amount being in excess of the nitrogen ingested. An increase in the amount of nitrogenous food taken into the system was followed by a proportionate rise in the amount of excreted nitrogen. These results are in opposition to some statements of Scheube and Durham, according to whom proteid metabolism in *kakke* patients is diminished. Careful urine analyses carried on in 43 cases of beriberi failed to show either albumen or sugar.

Duerck[11] has recently studied beriberi in Sumatra, and his histologic investigations confirm the description of the profound changes in the peripheral nerves and the skeletal muscles previously recorded by other writers. He advances the following hypothesis as to the cause of these lesions:

"The ubiquitous character of the degenerative lesions in the peripheral nerves and muscles and the absence of such changes in other organs compels one peremptorily to conclude that the harmful agent, acting in so specific a manner, can not be a living organism either of a vegetable or of an animal type. One can not, of course, exclude the possibility that the non-vital poison may enter the body, perhaps through the intestinal tract by the aid of a micro-parasite. However, if this be so, the absence of an obvious primary lesion or primary reaction is very striking. Lesions of the peripheral nerves caused by toxic substances are, of course, frequent. In this connection we may mention degenerations and inflammatory lesions due to alcohol, lead, arsenic, carbon bisulphide, ergotin, and other intoxicants; and it is also well known that substances formed in the body itself may, by processess of autointoxication, lead to lesions of the peripheral nerves."

Yamagiwa[12] has recently reaffirmed his former statements regarding the etiology of the disease in the following words: "Kakke or beriberi is an intoxication due to the daily use of boiled rice which has been improperly stored and preserved. The intoxication causes a contraction of the small arterial branches of the circulation. This again produces dilatation and hypertrophy of the heart, local anæmia of the skin, mucous membranes, peripheral nerves, muscles, and kidneys, and finally regressive metamorphoses in the tissues named."

Wright, in giving a summary of the theories regarding the etiology of the disease, mentions the following: (1) Gelbke's theory that beriberi is due to dry fish infected with a trichina; (2) that of M. Miura that it is due to the ingestion of certain kinds of raw fish; (3) Grimm's theory that it is caused by the ingestion of infected fish; (4) Takagi's that it is due to a pathogenic diet in which nitrogen is deficient; (5) Ross's that it is the result of arsenical poisoning; (6) the belief that it is due to the ingestion of moldy rice; (7) Braddon's theory that the ingestion of a specific organism which develops on growing rice causes beriberi; (8) Manson's that it is due to a place germ, and (9) Glogner's that it is produced by a hæmic plasmodium.

[10] These investigations have not been published. I am indebted to Professor Shiga, of the Tokyo Institute for Infectious Diseases, where they were carried on, for a communication concerning their result.

[11] Duerck: Ueber Beriberi, etc. *Münch. Mediz. Wochenschrift.* (1905), **52**, 1913.

[12] Yamagiwa (and Yamanowchi): Ueber das wesen der Kakke. *Salkowski Festschrift, Virchow's Archiv.*, **156**, 451.

Views other than the above in regard to the etiology of beriberi are that it is an anæmia of a pernicious type, that it is a modified and secondarily changed form of scorbutus, that it is due to carbon monoxide poisoning, or that it is caused by *Uncinaria duodenale* or by *Trichocephalus dispar*.

The following list gives the names of a number of investigators who have laid claim to the discovery of the specific micro-organism of beriberi: DeLacerda (a bacillus), Taylor (a bacillus), Rost (a bacillus), Ogata (a bacillus), Van Eecke (a coccus), Pekelharing and Winkler (a bacillus and a coccus), Wright (a coccus), Dangerfield (a coccus), Glogner (an amœba), Fajardo (a hæmatozoön), and Okata and Kokubo (a coccus).

Wright, in his studies on beriberi in the Malay Peninsula, noticed that although the disease is almost unknown among Europeans, a few authenticated cases had been reported during the last ten years. In the Malay Peninsula the disease occurs mainly among the Malays, Tamils, and particularly the Chinese, and the greatest number of cases is found in the prisons. This author's theory in regard to the etiology of beriberi is that it is due to a specific organism which gains entrance to the body by the mouth, develops chiefly in the pyloric end of the stomach and the duodenum, and produces a toxin, and that the latter being absorbed, causes atrophy of the peripheral terminations of the afferent and efferents neurons. He further believes that the specific organism is passed in the fæces and then lodges in the floors and walls of confined places through accident or through the careless personal habits of those affected by the disorder; whereupon, provided congenial meteorologic, climatic, and artificial conditions exist or there is close association from overcrowding, the organism becomes virulent and, gaining entrance to the healthy body by means of food, gives rise to an attack of the disease. Wright explains the fact that the germ remains so closely focal by its being at once destroyed by the action of direct sunlight; he also assumes that the presence of carbon dioxide or some other gas is necessary for its development in a virulent state. It seemed to him that the duration of the active stage of the organism in the body is between three and four weeks. He examined blood taken from 12 acute pernicious beriberi cases, from 36 simple acute ones, and from 27 in which a residual paralysis was existent, in order to detect the specific organism of the disease, if possible. The blood was first collected from the skin of the finger and lobe of the ear, and if a growth occurred in the culture media a second specimen was taken from the median cephalic vein at the elbow. The blood of 18 Chinese not infected with beriberi was examined by identical methods for control experiments. Wright concluded that the few organisms which developed in the cultures in these two series of investigations were contaminations derived from the skin and that they have no relation whatever to beriberi. Some of these organisms, Wright states, had previously been described by Pekelharing and Winkler and by Von Eecke, who had erroneously believed that they were associated with beriberi. It is interesting to quote freely from Pekelharing and Winkler, who have claimed to have discovered the specific cause of beriberi. They say: "In 15 cases we obtained a growth of bacteria; from 12 patients a growth of micrococci; from 3, one of rod-like bodies. The rods differed from each other in every instance. * * *

"In the 12 other cases the tubes inoculated with blood showed micrococci. These developed best on the solid substances, where they formed a white bed with a shining surface. This phenomenon was noticed in 10 cases but in 2 of the cultures a yellow color developed. * * * Sometimes different bacteria were cultivated from the same blood but this did not happen when agar-agar and blood serum were used as the media. * * * The different colonies which developed on the bed of gelatine did not at all resemble each other. On one occasion we found seven colonies of micrococci, of which two consisted of a white and five of a yellow

growth. * * * On several occasions we also noticed that, when we placed a little of the old, white growth of micrococci which had been kept for some months in a fresh soil of agar-agar, yellow growths of micrococci were developed which sometimes grouped themselves in tetrad forms. But we can not draw hasty conclusions from any of these observations. * * * Some further researches will be necessary to decide whether the different forms of micrococci which we obtained in our attempts at cultivation from the blood of sufferers from beriberi are of different species, or whether they are not varieties of the same one. Objections may be advanced that in these fifteen cases the bacteria did not occur in the blood, but that they were collected by an accidental contamination during manipulation and so entered the nutrient media."

It may be added that all of the animal experiments of the Dutch investigators were entirely inconclusive in character.

Stanley[13] examined the blood in 30 cases of beriberi occurring in Shanghai. In each instance 1 cubic centimeter of blood was collected under aseptic precautions from the median cephalic vein, and inoculated into various culture media. In all, 150 cultures were made. All the tubes excepting two remained sterile. These developed *Staphylococcus pyogenes aureus* and *Micrococcus tetragenus*. He also injected 1 cubic centimeter of blood from beriberi cases into each of six rabbits. These animal experiments and others in which moldy rice was employed were completely negative. Stanley concludes that the blood in beriberi is sterile and that the organisms found by Pekelharing and Winkler do not stand in any causal relationship to the disease. His experiments carried on with the object of detecting whether a specific toxin was present in the rice were likewise negative.

Ellis,[14] who had an opportunity in the government lunatic asylum of Singapore, of studying a large amount of beriberi, made a number of blood examinations in order to verify Pekelharing and Winkler's claims. However, he completely failed to find a bacillus in the blood, and his cultures made from the spleen, stomach, nerves, and other organs at post-mortem examinations likewise were negative.

Glogner,[15] whose work on beriberi is frequently mentioned, says that the disease is simply a multiple neuritis which is very common under tropical conditions, but which also occurs in Europe. He calls attention to the fact that whereas in Europe, when the symptoms occur in connection with diphtheria, typhoid, lead or alcohol poisoning, the etiology is generally obvious, in the Tropics the origin of the malady is as a rule not easily detected. This author examined the blood from the spleen of 98 cases of beriberi. He claims that in 63 he found extra-globular bodies rich in pigment, which were different from the hæmaœba of malaria. Glogner regards these bodies to be the specific cause of beriberi.

Fajardo[16] has claimed the discovery of another protozoön in the blood of beriberi patients which is very similar but not identical with the malarial parasite. He also regards this organism as the specific cause of the disease.

Rost[17] observed an outbreak of beriberi in the Meeklita gaol, India, and which occurred at about the same time that a disease attacked pigeons in the vicinity

[13] Stanley: The Nature of Beriberi. *Journal of Hygiene* (1902), **5**, 369.

[14] Ellis: A Contribution to the Pathology of Beriberi. *London Lancet* (1898), **2**, 985.

[15] Glogner: Ein weiterer Beitrag zur Aetiol. der mult. Neuritis in den Tropen. *Virchow's Archiv.* (1895), **141**, 401.

[16] Fajardo: Von der Haematozoarie der Beriberi und deren Pigment. *Centralbt. für Bacteriol.* (1898), 1 Abt., **24**, 558.

[17] Rost: The Cause of Beriberi. *Brit. Med. Journ.* (1902), **2**, 835.

and caused paralysis of the wings and death among these birds. He believes the cause of beriberi to be an angular diplobacillus, which is extremely resistant to heat, a temperature of 220° F. acting for nine hours being necessary to kill the spores. He claims to have found this same organism in the blood and in the cerebro-spinal fluid of a large number of beriberi cases. From blood, it could be cultivated in broth, rice broth, and in ascitic fluid. It was very motile and about the size of the tubercle bacillus. The organism was found in moldy rice as well as in the blood of beriberi patients. He believes that with it he could produce in fowls, both by feeding and inhalation, a disease exactly similar to beriberi in man.

Durham performed a number of experiments with the view of producing in monkeys, guinea pigs, and rabbits a disease similar to or identical with beriberi. His experiments included the feeding of dry fish and rice, injection of serum from beriberi cases, the administration by the mouth to monkeys of the contents of the gastro-intestinal tract of beriberi cases, to monkeys of dust from infected localities, inoculation from throat to throat in monkeys, and attempts to infect with bedbug bites. All the experiments were obsolutely negative. Durham severely criticises Wright's claim of having produced beriberi in monkeys by confining the animals in prison cells where the disease had constantly been prevalent in man, and by feeding these animals with food mixed with the dust from such cells. He says that the neuritis observed in Wright's monkeys was due to septic absorption from old, chronic ulcers and he further states that he himself observed the nerves in an advanced state of degeneration in monkeys showing septic processes. Durham is inclined to regard the tonsils as the portal of entrance of the specific virus of beriberi, and with reference to this point he says: "Clinical observations of throats in two places, * * * Gopeng Perak and Christmas Islands, more than 1,000 miles apart, as well as in Kuala Lumpur, seem to indicate that in early cases and in those which had recently come to hospital there was a marked faucial redness. This condition was not associated with tenderness or swelling of the lymphatic glands. Sterilized cotton, wood swabs mounted on wires were smeared on the throats of a number of patients and then on the surface of agar media in Petri dishes. After twenty-four hours, or better after forty-eight hours, remarkable numbers of small, low, translucent colonies appeared on the plates. After ninety-six hours they measured only about 1 millimeter in diameter. Under a low power of the microscope they showed a well-marked, distinguishing feature in that there were tiny loops of projecting organisms around the periphery. Some plates were crowded with these small looped colonies, and this almost or quite to the exclusion of other kinds of colonies. Morphologically they assumed a somewhat streptococcal appearance being grouped in short chains but there was a great tendency to the formation of involution forms of a swollen, irregular, or rod-like character; no motility, stained by Gram's method."

However, Durham did not succeed in isolating the same organisms from the dust of the cells, nor did he obtain it from the intestinal tracts of bodies dead of beriberi. His attempts to propagate this organism in the second generation failed. He found no evidence that mosquitoes or cockroaches spread the disease. Durham believes that the dietetic or physiologic theory, the one of unsound food, or of arsenical poisoning all appear to be insufficient to account for the spread of the disease. His own observations prompt him to believe that beriberi is communicated more or less directly as an actual infection from person to person, or through fomites.

Tetamore[18] reports an epidemic among native prisoners in the United States

[18] Tetamore: *Surgeon-General's Report for the Fiscal Year ending June 30, 1901;* Washington (1901), 236.

military prison, Lingayen, Pangasinan, P. I. This outbreak occurred between October, 1900, and January, 1901. There were 141 persons attacked by beriberi, of which 31 died. Bacteriological examination of the blood was made in 35 cases. The results, in general, were negative but in a few cases micrococci were found which were not regarded as specific in their nature.

From the above statements it appears that the most careful attempts to obtain a specific organism from the blood of beriberi cases have been negative. It may also be mentioned that Robert Koch was unsuccessful in isolating any specific bacterium.

Dangerfield[19] has recently published a very elaborate report of 400 pages on beriberi. On page 59 of his book he says: "Since 1897 I have been impressed with the constancy of digestive disturbances in all cases of beriberi, manifesting themselves in the form of anorexia, gastralgia, vomiting, nausea, dyspepsia and epigastric pain on pressure. We have therefore studied this question carefully in the living as well as in the cadaver. Later, we have intubated many patients with Fauche de Beouf's stomach tube, in order to examine the gastric contents. In almost all of our cases we have found cocci, both by the direct microscopical examination and by making cultures in Jensen's fluid, after neutralizing the gastric contents. Therefore, it is this method which one should preferably use in searching for the beriberi coccus in the living. The pathological-anatomical lesions of the gastro-intestinal tract are so characteristic that we have questioned how it could be possible for them to have escaped the attention of other observers. The bacterium of beriberi belongs to the family *Coccaceæ* and to the genus *Micrococcus*. It appears in the form of a spherical, perfectly round, isolated cell. However, this form varies according to the stage of evolution of the bacterium."[20]

Dangerfield states that the organism is found on the epidermis, in the soil, in the air, in water, in the sputum, in vomited matter, and in the fæces, as well as in the intestinal tract, in the stomach, and in the small intestine. Round cells from 0.2 to 1.5 μ. Very unstable in virulence. Grow well at from 22° to 45° C. Do not live at 0° or above 100° C. They are obligate aërobic. Grow rapidly at 37° C. on agar; however, during the first twenty-four hours, slowly. Odor is disagreeable. No evolution of gas. Stain with difficulty by Gram's method. Slowly decolorize by acid alcohol. Give indol reaction in young bouillon cultures. Do not give the cholera-red reaction. Culture media are always alkaline in all stages of growth. Bouillon becomes very slightly clouded with a slight film around the edge of the surface. There is formed a milky, non-viscous, white deposit. Grows poorly in glucose bouillon. On Roux plates the cultures are white, shiny, creamy, and porcelain-like, with fringed margins and with a paler color. Gelatin is liquefied slowly. Liquefaction does not begin before the fourth day. On agar the coccus grows poorly at 18° to 20° C. The cells are small. On Jensen's rice the colonies are white, peculiar, porcelain-like, cream-like, abundant. On potato there is formed a beautiful, white, opaque, porcelain-like growth, visible after forty-eight hours. On carrots, the growth is very poor, showing degenerate cocci. On artichoke, the growth is good and gives after the first day a beautiful, green color. It grows well in ascitic fluid. It gives beautiful, white cultures on solidified blood serum. It grows in milk without coagulating it.

The most recent claim of the discovery of a specific germ for beriberi is made by Okata and Kokubo, two Japanese army surgeons, who have had an excellent opportunity to study the extensive outbreak of beriberi occurring among the

[19] Dangerfield: *Le Beriberi*, Paris (1905).

[20] For a complete description of the bacterium the reader is referred to the original paper.

Japanese soldiers transferred from Manchuria to Japan during the recent Russo-Japanese war. These investigators have isolated a coccus, which generally assumes the shape of a diplococcus but which may also at times present itself as a staphylococcus. They confidently maintain that this organism is the causative factor in beriberi.

The author, working in the Hiroshima Kakke Hospital under the direction of Surgeon-Major Kokubo, has had an opportunity to isolate this identical organism from cases among soldiers suffering from beriberi in Hiroshima. A translation of Okata and Kokubo's first description of the micro-organism, which they claim to be the etiologic factor in *kakke,* has already been published in a previous number of this Journal.[21]

THE THEORY OF ARSENICAL POISONING AS THE CAUSATIVE FACTOR OF BERIBERI.

Among the theories brought forward to explain the etiology of beriberi is that of arsenical poisoning. I shall consider it somewhat in detail. A number of observers who have made beriberi a subject of special inquiry have noticed the frequency of this affection among workers in tin mines. Occasionally, there has been a tendency to regard the disease as a direct manifestation of arsenical poisoning.

Recently, Donald Ross[22] has become an advocate of this theory. He calls attention to the fact that the clinical symptoms of certain cases of beriberi are extraordinarily similar to those shown by the victims of chronic arsenic poisoning which occurred in Chester and Manchester (England) in 1900 and which were characterized by a multiple, peripheral neuritis; in fact, they resembled what appeared to be cases of epidemic, peripheral neuritis. Following out this theory, Ross[23] later reported a case of beriberi which clinically presented features similar to those met with in the dry, paralytic form of the disease; it also resembled the cases of arsenic poisoning observed in England in 1900. Professor Dixon Mann examined a lock of hair from this patient and reported that he found a considerable amount of arsenic. No arsenic had been administered medicinally.

Enlarging upon his researches in this direction, Ross[24] procured twenty samples of hair from beriberi patients, mostly Chinese, from the Penang General Hospital. These were also analyzed by Dixon Mann, who reported that 6 out of the 20 samples contained arsenic; two yielded more than a trace; and two each a decided and a minute trace. The positive samples were nearly all from recent cases of beriberi, the negative ones as a rule from the older ones. Ross draws the following conclusion from the result.

"The probability is very strong that the Penang beriberi is arsenical, especially when we know that the people there largely work in tin manufactories and are brought closely into contact with arsenic."

[21] *Phil. Journ. Science* (1906), 1, 169.

[22] Ross: Beriberi and Chronic Arsenical Poisoning. *London Lancet* (1900), 2, 1677.

[23] Ross and Reynolds: A Case of Beriberi Probably due to Arsenic Poisoning. *Brit. Med. Journ.* (1901), 2, 979.

[24] Ross: Arsenic in the Hair of Beriberi Patients from Penang. *Brit. Med. Journ.* (1902), 1, 329.

Further researches are given in a subsequent report[25] by the same author. Eight samples of the hair of beriberi cases were procured by him from the Singapore Asylum. The analyses made by Mann showed arsenic in the hair from three recent cases and none in the five samples from older cases. Ross further concludes that: "Whatever the truth may ultimately prove to be, the analyses which Prof. Dixon Mann has made seem to suggest that the arsenic, after producing the characteristic neuritis, has gradually disappeared from the hair in some manner, or has, perhaps, been cut away as convalescence has advanced."

Manson (1. c.) in referring to the arsenical poisoning theory of beriberi calls attention to the fact that the mere presence of traces of arsenic in the hair of persons suffering from beriberi could hardly be advanced as a conclusive argument of such an origin of the disease. While he is not prepared to deny the frequent occurrence of arsenical neuritis in the Tropics, he feels quite certain that what is generally considered as beriberi has nothing to do with arsenic and does not represent an arsenical neuritis.

Dunham (1. c.) believes that the results of the analyses reported by Ross, in which only traces of arsenic were discovered, really oppose the arsenic hypothesis and do not support it. He points out that out of many hundred beriberi cases he encountered but one of herpes, such as is frequently found in arsenical intoxication. While arsenic may be and is partaken of by many who are afflicted with beriberi as well as by others, the analyses which have been made are against the supposition that there is a connection between the two (clinically more or less distinct) conditions of arsenical neuritis and beriberi. Upon Dunham's suggestion, arsenic was given to a number of beriberi patients in large doses. No favorable result was observed from this treatment, but several cases recovered in spite of the heroic doses administered.

The question whether arsenic is or is not a normal constituent of the human body is at present open to argument.

A. Gautier[26] claims that in 200 tests he has always found arsenic in the thyroid gland and in the skin and its appendages. His observations are confirmed by other French writers, viz: Lapierre, Pagel Imbert, Badel, and Bertrand. However, Gautier's statements are contested and the presence of arsenic as a normal constituent of the thyroid and the skin is denied by Hoedelmoser,[27] Cerny,[28] and Ziemke.[29] The first-mentioned author, in his tests, adopted Gautier's tedious method of digesting and oxydizing 100 grams of the tissues to be tested with 30 to 60 cubic centimeters of nitric acid and 1 cubic centimeter of sulphuric acid, in order to prevent any possibility of losing arsenic by volatilization. In spite of these precautions he could not detect arsenic and consequently refers the results of the French observer to impure reagents.

In order to test the validity of Ross's claim, hair from some of our beriberi patients was analyzed. The samples were taken from the heads of ten native Filipinos, as follows:[30] One from a fatal case of acute, wet

[25] Idem.: Some More Instances of the Presence of Arsenic in the Hair of Early Cases of Beriberi. *Brit. Med. Journ.* (1902), **2**, 837.

[26] Gautier: Sur l'arsenic normal des animaux. *Comp. Rend. hebd. Soc. Biol.* Paris (1902), **54**, 727; also Existence normal et origine de l'arsenic, etc., ibid., 1242.

[27] Hoedelmoser: *Zeitschr. für Physiol. Chemie.*, **33**, 329.

[28] Cerny: *Ibid.*, **34**, 408.

[29] Ziemke: *Deutsche Apotheker Ztg.* (1902), **17**.

[30] The analyses were made in the Chemical Laboratory of this Bureau, the first in 1904 by C. L. Bliss, the last nine by L. A. Salinger, to both of whom I wish to express my thanks.

beriberi, one from a fatal case of acute pernicious beriberi, and eight from cases of subacute or chronic beriberi.

The first sample was shown to be negative by Mr. Bliss, but in order absolutely to check his result, the remaining nine were carefully tested for arsenic, the method used having the following main features: From samples 1 to 9, about 1 gram of each was used for the determination; from the remaining one, 0.5 gram was employed. Organic matter was destroyed in the usual way, the solution then diluted, filtered, and evaporated with sulphuric acid, this operation being repeated several times after the addition of a small amount of nitric acid, until the fumes of sulphuric acid appeared. After all organic matter had been destroyed, the test for arsenic was made in a small Marsh apparatus. No trace of arsenic could be detected in any of the samples; a control by this method was sufficiently delicate to detect 0.01 milligram.

The ten samples of hair from beriberi patients on analysis, therefore, demonstrated the absence of arsenic.

ANIMAL EXPERIMENTS WITH THE OKATA-KOKUBO COCCUS.

During the past six months I have extensively studied the Okata-Kokubo coccus and the relation it bears to beriberi. The results of these experiments and of the investigations undertaken to find this identical organism in beriberi cases occurring in the Philippine Islands may be summarized as follows:

Six strains were selected for cultural and animal experiments. Three were isolated by Professor Okata from beriberi autopsies; one was a culture grown by Professor Kokubo from the urine of a *kakke* patient and two were isolated by myself from the urine of *kakke* patients in Hiroshima, in which place I was working under the direction of Professor Kokubo. One of the last two cultures exclusively showed cocci of the large type. The six strains were grown on the following media: agar, alkaline to litmus; agar, alkaline to phenolphthaleïn; glucose-agar; litmus-lactose-agar; litmus-milk; bouillon alkaline to litmus; bouillon, alkaline to phenolphthaleïn; Dunham's peptone solution; gelatine; potatoes. All the cultures were kept in the incubator between 34° to 36° except the gelatine tubes which were maintained at a lower temperature.

A study of the growth of the different strains on the variety of culture media employed, in general confirmed the description given by Okata and Kokubo in their first paper. However, a few minor differences were noticed. These were as follows:

Examination of gelatine cultures during the first two weeks showed no liquefaction.

After twenty-two days on this medium the following conditions were noticed:

Stem Kokubo, heavy growth, superficial liquefaction;

Stem Herzog (large cocci), scanty growth, no liquefaction.

Stem Herzog, very abundant growth, liquefaction.

Stems Okata, I, II, and III, scanty growth, no liquefaction.

Non-inoculated control tube. No liquefaction.

After fifty-six days:
Stem Kokubo. Abundant growth. Very advanced liquefaction.
Herzog (large), scanty growth, no liquefaction.
Herzog I, very advanced liquefaction, like stem Kokubo.
Okata I, II, III, no liquefaction.
Control tube, no liquefaction.

The original communication states that the *kakke* coccus grows in milk without coagulating the casein. Our tests in this respect show:

After twenty-two days' growth in litmus milk:
Stem Kokubo, media fluid, red, little coagulation.
Herzog (large), fluid, red, moderate coagulation.
Herzog I, fluid, red, marked coagulation.
Okata I, II, III, fluid, red, very little coagulation.
After 56 days, all litmus milk tubes were red and the degree of coagulation was as follows:
Kokubo, moderate coagulation.
Herzog (large), marked coagulation.
Herzog I, marked coagulation.
Okata I, II, III, marked coagulation.

Therefore, after a longer period of growth, all stems showed marked acid formation and a varying degree of casein coagulation. The control tube after fifty-six days had shown no changes. On the other media the cultures presented the features already described by Kokubo and Okata. None of them formed any gas in glucose or lactose media.

The following animal experiments were made:

First series.—On November 20, 1905, twelve monkeys (species *Macacus cynomolgus*) were inoculated with the 6 stems, as follows:

Animal number.	Date.	Amount.	Culture.	Stem.
Monkey No.—		*c. c.*		
1473	Nov. 20, 1905	1	5-day-old bouillon culture, second generation of original Japanese culture, intraperitoneally.	Kokubo.
1474	do	1	do	Do.
1475	do	1	do	Herzog (large).
1476	do	1	do	Do.
1477	do	1	do	Herzog I.
1478	do	1	do	Do.
1481	Nov. 22, 1905	1	2-day-old bouillon culture, second generation of original Japanese culture, intraperitoneally.	Okata I.
1482	do	1	do	Do.
1483	do	1	do	Okata II.
1511	do	1	6-day-old bouillon culture, second generation of original Japanese culture.	Herzog I.
1512	do		do	Herzog (large).
1513	do		do	Kokubo.

These monkeys were kept under observation during fifty-two days. They never developed fever, paralysis, swelling of the lower extremities, difficulty of respiration, nor any of the other symptoms of beriberi. They were, in fact, never otherwise than well, they ate normally during this period, and were discharged from observation on January 12, 1906.

Second series.—On March 15, 1906, twelve monkeys (species *Macacus cynomolgus*) were inoculated with the 6 stems, each animal receiving intraperitoneally 2 cubic centimeters of a 9-day-old bouillon culture. The animals were of both sexes, and included young and full-grown individuals.

Animal number.	Amount.	Stem.
Monkey No.—	*c. c.*	
1836	2	Kokubo.
1837	2	Do.
1838	2	Okata I.
1839	2	Do.
1840	2	Okata II.
1841	2	Do.
1842	2	Okata III.
1843	2	Do.
1844	2	Herzog I.
1845	2	Do.
1846	2	Herzog (large).
1847	2	Do.

These animals were kept under observation for over one month. They remained perfectly well during this time.

Third series.—Twelve half-grown guinea pigs were inoculated on February 26, 1906, as follows: Three standard *oesen* of a 6-day-agar culture were suspended in 10 cubic centimeters of physiological salt solution. Each guinea pig received 1 cubic centimeter of this suspension intraperitoneally or subcutaneously, as shown by the following table:

Animal number.	Amount.	Stem.	Inoculation.
Guinea pig No.—	*Standard oese.*		
1806	0.3	Okata I	Intraperitoneally.
1807	.3	do	Subcutaneously.
1808	.3	Okata II	Intraperitoneally.
1809	.3	do	Subcutaneously.
1810	.3	Okata III	Intraperitoneally.
1811	.3	do	Subcutaneously.
1812	.3	Kokubo	Intraperitoneally.
1813	.3	do	Subcutaneously.
1814	.3	Herzog I	Intraperitoneally.
1815	.3	do	Subcutaneously.
1816	.3	Herzog (large)	Intraperitoneally.
1817	.3	do	Subcutaneously.

The animals were kept under observation for nearly two months. They remained well and did not develop any disease.

Fourth series.—On March 15, 1906, twelve young guinea pigs were inoculated intraperitoneally, each with 1 cubic centimeter of a 9-day-old bouillon culture of the different stems, as follows:

Animal number.	Amount.	Stem.
Guinea pig No.—	*c. c.*	
1893	1	Kokubo.
1894	1	Do.
1895	1	Okata I.
1896	1	Do.
1897	1	Okata II.
1898	1	Do.
1899	1	Okata III.
1900	1	Do.
1901	1	Herzog I.
1902	1	Do.
1903	1	Herzog (large).
1904	1	Do.

These animals were kept under observation for over one month. They remained well.

Fifth series.—On March 15, 1906, twenty-four young rabbits were inoculated, each receiving intraperitoneally 1 cubic centimeter of a 9-day-old bouillon culture of one of the 6 stems.

Animal number.	Amount.	Stem.
Rabbits Nos.—	*c. c.*	
1869–1872	1	Kokubo.
1873–1876	1	Okata I.
1877–1880	1	Okata II.
1881–1884	1	Okata III.
1885–1888	1	Herzog I.
1889–1892	1	Herzog (large).

The twenty-four animals were kept under observation for over one month. They remained perfectly well.

Sixth series.—On March 16, 1906, twenty-one rats (mostly of the species *Mus decumanus* but also a number of *M. rattus*) were inoculated intraperitoneally, each receiving a 9-day-old bouillon culture, as follows:

Rats Nos. 1848 to 1859 each 1 cubic centimeter of stem Kokubo, and rats Nos. 1860 to 1868 each the same amount of Okata No. II.

March 22, a. m. Rat No. 1848 died during the previous night. Body not yet putrid, very much emaciated. On section a grayish white floccule, the size of a millet seed, was found on the surface of a loop of the small intestine;

otherwise no pathological changes were observed. The floccule was composed of leucocytes and endothelial cells, and contained innumerable, small diplobacilli. Cultures were made from this floccule and from the spleen and heart's blood. The tubes inoculated from the floccule developed a small bacillus, but no cocci. The small intestine of this animal had evidently been wounded during the intraperitoneal inoculation. The cultures from the spleen and heart's blood were negative.

March 27, 1906. Rat No. 1849 was found dead in the morning. Body much emaciated, already decidedly putrid. On post-mortem examination there was found a caseous abscess the size of a very small hazelnut in the anterior body wall opposite the lower ribs of the left side. This abscess contained many slender, non-acid proof bacilli. Tubercle bacilli were not found.

The following rats died subsequently: No. 1860, March 27; No. 1861, March 27; No. 1863, March 28; No. 1856, April 7; No. 1859, April 10. Smears from the different organs and inoculations of culture media were made from each animal. In no case was it possible to regain from the tissues the cocci which were inoculated on March 15, and there appears to be no doubt that the inoculated organism had nothing to do with the death of the experimental animals. It may be stated that a number of the laboratory rats not inoculated but living under the same conditions, died at about this time. The other animals of this series inoculated with the *kakke* coccus remained alive; none of them developed any symptoms of beriberi.

BLOOD EXAMINATIONS OF BERIBERI CASES IN MANILA.

Blood examinations in twelve cases of beriberi were made by the author during the years 1904 and 1905 with the object of obtaining the specific micro-organism of the disease from the blood, if it was present therein. These examinations gave a negative result and no detailed record of them has been preserved. Since my return from Japan, over forty additional blood examinations have been made, and detailed records of these have been kept. On December 7 and 9, 1905, 39 male inmates of Hospital B of Bilibid Prison, who were suffering at this time with all types of beriberi except that of the most acute, pernicious variety, were examined. Some of the cases were of the wet, hypertrophic type, others of the dry and atrophic variety; in certain ones all of the more prominent symptoms of beriberi were still present; in others, convalescence was well advanced. These blood examinations were undertaken with the assistance of Mr. Charles B. Hare, at that time a member of the staff of the Biological Laboratory.

The method of procedure was as follows:

The skin over the median cephalic vein of the elbow was cleansed with soap and water, bichloride solution, and alcohol. The vein was then pierced with a hypodermic syringe needle and from 1 to 2 cubic centimeters of blood withdrawn and at once injected into a 100-cubic-centimeter flask containing 50 cubic centimeters of slightly alkaline bouillon. The cultures were then incubated at 37° and kept under observation for several weeks.

Thirty-three of the flasks remained permanently sterile. In six, a growth developed in which the following organisms were isolated.[31]

Culture No. 2 developed a coccus, No. 4 a staphylococcus, No. 13 a large staphylococcus, No. 19 a spore-bearing bacillus, No. 26 a large diplococcus, and No. 37 a medium-sized, slender, spore-forming bacillus. All of the above stained well by Gram's method.

The four varieties of cocci which were obtained have not as yet been very extensively examined as to their cultural properties. However, none of them seem to be identical with the cocci brought from Japan, and experiments made with them with the object of producing beriberi in animals have all been negative, as will be seen from the following table:

Seventh series.—Twelve monkeys, each received intraperitoneally one-fifth of an oese of an agar culture in 1 cubic centimeter of physiological salt solution, as follows:

Monkey No.—	Organism isolated from Bilibid beriberi case No.—	Monkey No.—	Organism isolated from Bilibid beriberi case No.—
1655	2	1661	13
1656	2	1662	13
1657	4	1663	26
1658	4	1664	26
1659	19	1665	37
1660	19	1666	37

These monkeys were well during the days following the injections and they neither developed symptoms of beriberi nor manifested appearances of any disease.

In a case of hypertrophic beriberi,[32] which quickly terminated fatally, a blood examination was made January 26, 1906, five days before death. (See necrospy No. 1636, page 747 of this article.) At this time the patient presented all of the symptoms of an acute and profound case of beriberi. The examination included anaërobic cultures.

About 5 cubic centimeters of blood were withdrawn from the median cephalic vein. Two flasks containing 50 cubic centimeters of bouillon were inoculated, each with 1 cubic centimeter of blood. One was kept aërobically, and the other in a hydrogen atmosphere, anaërobically. Several agar tubes were likewise inoculated from the blood, some of which were also developed aërobically, and some anaërobically (Buchner's pyrogallic acid method being used). The cultures were left under observation during from four to five weeks. They remained permanently sterile.

Apparently, all of the cultures from this case had remained sterile, but the possibility was considered that perhaps something ultramicroscopic in character and which did not give rise to any changes in the culture media, detectable by either ordinary macroscopic or microscopic examina-

[31] The cultures are designated by the same numbers under which the 39 cases of beriberi were recorded.

[32] Occurring in the Civil Hospital.

tions, might have developed. Hence, 6 monkeys were inoculated from the culture media, which had been kept both aërobically and anaërobically.

Eighth series.—

Animal number.	Date.	Amount.	Culture.
Monkey No.—		c. c.	
1717	Feb. 2, 1906	1	Aërobic culture A.
1718	do	1	Anaërobic culture A.
1719	do	1	Aërobic culture B.
1720	do	1	Anaërobic culture B.
1721	do	1	Aërobic culture D.
1722	do	1	Anaërobic culture D.

These animals never showed any sign of disease and remained permanently well.

Before the bouillon cultures from the above case of beriberi were used for inoculating the animals recorded in the preceding tables, subcultures from the tubes were made on agar. These were preserved in the incubator both under aërobic and anaërobic conditions. After four weeks it was noticed that each of two of the tubes had developed a single colony. The one which had been kept under anaërobic conditions contained large, yellow cocci, which later also grew aërobically; the aërobic tube showed a dirty, grayish-brown, very tenacious colony composed of bacilli, which stained very irregularly, and appeared morphologically somewhat like diphtheria bacilli from an older culture. After transplanting a portion of this growth to a fresh agar tube the remainder of the colony was rubbed up with 15 cubic centimeters of sterile salt solution; with this very imperfect suspension, which contained comparatively large flocculi, six monkeys were inoculated, each with about 1.3 cubic centimeters of fluid.

Ninth series.—

Animal number.	Date.	Suspension.
Monkey No.—		c. c.
1825	Mar. 7, 1906	1.30
1826	do	1.30
1827	do	1.30
1828	do	1.30
1829	do	1.30
1830	do	1.30

The animals remained permanently well.

Cultures were made from the internal organs in a number of post-mortem examinations of beriberi cases and examined with the view of ascertaining whether the identical coccus brought from Japan was present. Most of these were negative. An acute case of beriberi died at Bilibid

Hospital after an illness of only a few hours and the necropsy (No. 1634) was performed two hours after death. Cultures taken from the very much enlarged spleen developed colonies of a pale-yellowish diplococcus which, in most media, showed considerable similarity to the cocci brought from Japan. From these cultures five rabbits were inoculated.

Tenth series.—Three of the animals (1747, 1748, 1749) received intraperitoneally 1 cubic centimeter of a 2-day-old bouillon culture, and two (1750 and 1751) received subcutaneously 1 cubic centimeter of the same culture. These animals, which were under observation for two months, never showed any signs of disease and remained permanently well.

In order to prepare an anti-serum for the purpose of making agglutination tests, other rabbits were inoculated with the Kokubo coccus in successively increasing doses. All of these animals remained well. One of the rabbits, when finally bled, after having been injected at intervals on numerous occasions during a period of seventy-eight days, furnished a serum of only very low agglutinating power.

On March 7, 1906, a post-mortem examination (No. 1674) was made upon the body of a young Japanese who had been ill but a few days. The clinical diagnosis of acute, pernicious beriberi was confirmed at autopsy. During this examination two agar tubes were inoculated from the cerebro-spinal fluid obtained by puncture at the third lumbar vertebra with a sterile syringe, and another was inoculated from the heart's blood. Pieces of the wall of the stomach and of the duodenum, together with some of the gastric contents, were placed in a flask containing several hundred cubic centimeters of alkaline bouillon the latter was then heated to 80° C. and kept at that temperature for about ten minutes. It was then cooled in the refrigerator and subsequently incubated. It developed a spore-forming bacillus. The tube inoculated from the heart's blood remained permanently sterile, and the tubes inoculated from the cerebro-spinal fluid developed colonies of different bacilli, evidently contaminations.

Monkeys and rabbits were inoculated on March 26, 1906, with the cultures obtained from the above necropsy (No. 1674), after the latter had grown in the incubator for nineteen days. Of the bouillon culture 1.5 cubic centimeter was injected intraperitoneally, of the agar cultures six normal oesen were rubbed up with 20 cubic centimeters of salt solution, and each animal received intraperitoneally 1.5 cubic centimeters of this suspension, as follows:

Eleventh series.—(March 26.)

Animal number.	Quantity.	Culture.
	c. c.	
Monkey No. 1916	1.5	From stomach.
Monkey No. 1917	1.5	Do.
Rabbit No. 1918	1.5	Do.
Rabbit No. 1919	1.5	Do.
Monkey No. 1920	1.5	Cerebro-spinal 1.
Monkey No. 1921	1.5	Do.
Rabbit No. 1922	1.5	Do.
Rabbit No. 1923	1.5	Do.
Monkey No. 1924	1.5	Cerebro-spinal 2.
Monkey No. 1925	1.5	Do.
Rabbit No. 1926	1.5	Do.
Rabbit No. 1927	1.5	Do.

One rabbit (No. 1919) and one monkey (No. 1917), which had received 1.5 cubic centimeters of the bouillon culture obtained from the stomach, died.

Monkey No. 1917 was found dead March 29. The post-mortem examination revealed nothing characteristic; smears from the organs showed a very small diplococcus, absolutely unlike the Okata-Kokubo coccus both in morphology and in cultural properties.

Rabbit No. 1919 was found dead on March 30. The autopsy showed a peritonitis with blood-tinged fluid in the abdominal cavity; the liver contained numerous microbic foci. The cultures inoculated from the organs developed a large, spore-forming bacillus, staining by Gram's method.

SPECIAL PATHOLOGY.

Baelz, Scheube, N. Miura, Yamagiwa, and Pekelharing and Winkler have particularly advanced our knowledge of the special pathology of beriberi.

Pekelharing and Winkler,[33] after giving due credit to Baelz and Scheube for having first shown that the principal seat of the disease in beriberi is the peripheral nervous system, point out that the changes in the nerves are not of the nature of an inflammatory, but of a degenerative, process. Their conclusions read as follows:

"Anatomical examination is in perfect accord with the inference drawn from clinical observation, that beriberi is a multiple neuritis. An extreme and very extensive affection of the peripheral nerves predominates, and as one approaches the central nervous system, the pathological evidence of nerve change diminishes. The anterior roots of the spinal nerves are always healthy; but in the posterior roots one sometimes meets with a slight atrophy of the fibers, which is always infinitely less on the proximal side of the intervertebral ganglion than on the distal prolongation of the nerve. In the spinal cord some variations of secondary importance are met with in the large nerve cells of the anterior cornua, but more constant still is a slight loss of fibers in the extension of the posterior roots in the two radicular zones, unaccompanied by any swelling of the axis cylinder, granular degeneration of cells, or multiplication of nuclei. We consider that we have established the claim that beriberi should be ranked among the diseases that are described under the name of multiple peripheral neuritis. However highly we esteem the work done by Baelz and Scheube, we consider that the proof has only now been given by us, inasmuch as we have clearly demonstrated that the nerves are attacked in the very first phase of the disease, and our anatomical observation has undoubtedly confirmed this affection of the nerves in a very great number of cases. In every beriberi patient some symptoms of degeneration, as well as of regeneration, in the peripheral nerves can often be found."

Pekelharing and Winkler also demonstrated that beriberi is not a form of pernicious anæmia, as had previously been claimed. They made a number of systematic blood examinations and proved that neither an oligocythemia nor an oligochromæmia of a marked degree was present. A number of other authors (among them Wright) have later confirmed the results of their investigations in this respect. Wright estimated the hæmoglobin and made blood counts in 26 cases of beriberi. A moderate anæmia was found in several cases. The number of red-blood corpuscles varied from 4,600,000 to 6,120,000, and the leucocytes from 6,720 to 7,600.

[33] Pekelharing and Winkler: *Beriberi*, English edition (1893), London.

Yamagiwa,[34] after a study of a large autopsy material, enumerates the most important pathologic changes in beriberi as follows: (1) Dilatation and hypertrophy of the right ventricle, and dilatation of the left; fatty metamorphosis of the myocardium; (2) degeneration of the peripheral nerves; (3) atrophy and degeneration of the skeletal muscles; (4) parenchymatous degeneration of the kidney; (5) hydrops. In other words, all the pathological changes in *kakke* are regressive in nature, with the single exception of the hypertrophy of the myocardium.

Yamagiwa, assisted by Yamanouchi,[35] recently has investigated the claim of Glogner—i. e., "that beriberi is primarily a disease of the heart and skeletal muscles (fragmentation) with a loss of continuity of the elastic tissue of the vessels, particularly of the pulmonary artery and its branches." The Japanese authors from their histologic studies conclude that Glogner's statements are not at all tenable and that the elastic fibers of the pulmonary artery and its branches are practically intact in beriberi.

In seven beriberi necropsies Plehn (l. c.) found the liver in six presenting the changes of interstitial hepatitis and in one, those of chronic congestion with secondary induration. This observer is therefore inclined to look upon the interstitial hepatitis as an important morbid change in beriberi.

Hermann Duerck,[36] who also has recently studied beriberi in Sumatra, states that the surrounding connective tissue, the fine connective tissue—i. e., the endoneurium—the myelin sheath, and even the axis cylinders of the nerves are all affected and that alterations are to be found even in acute cases. In the instance of a Chinese coolie, sick only fourteen days, who complained mainly of dyspnœa and palpitation of the heart, disturbances of locomotion increasing almost to complete paralysis were present. In this case sections of the vagus nerve showed almost complete degeneration of the myelin sheath, with irregularly fringed fragments, or with fragments resembling portions of a rosary. In other places the axis cylinders were entirely devoid of their myelin sheaths, many of which were found collapsed and with the neurolemma nuclei increased. The axis cylinders were spirally twisted, irregularly undulating, and in some places even broken up into fragments. The heart in the same case was dilated and resembled a flabby, thin-walled sac. Microscopically, the myocardium showed most extensive changes. The muscle cells were attenuated, having been pushed apart by a homogeneous, glassy mass, in which small, undulating clefts containing cell nuclei surrounded by some granular protoplasm were occasionally seen. A high magnification revealed the fact that this homogeneous substance was a degeneration product of the fibrils of the heart muscle cells. In many places there could very distinctly be seen a direct transition of the striped substance into the hyaline mass. The muscle cells were also separated longitudinally into a number of fine, parallel bands. This process resulted in the picture of free nuclei surrounded by a small amount of granular sarcoplasm. The bands evidently had undergone hyaline degeneration and the hyaline material included the nuclei, with a small amount of sarcoplasm. According to the report, the degeneration of the nerves could be followed step by step by the melting of the hyaline sheath, vacuolation, and the formation of honeycombed or foamy masses. Large cells, evidently leucocytes loaded with some of the degenerated hyaline, were found in the immediate neighborhood of the capillaries which supply the endoneural connective

[34] Yamagiwa: Beitrage zur Kenntniss der Kakke. *Virchow's Arch.* (1899), **156**, 451.

[35] Yamagiwa and Yamanouchi: Ueber das Wesen der Kakke. *Salkowski Festschrift.*

[36] Duerck: Ueber Beriberi, etc. *Münch. Mediz. Wochenschr.* (1905), **52**, 1913.

tissue. The neurolemma nuclei were enlarged and proliferated, and the proliferating endoneurium had given rise to fibrous tissue. The voluntary muscles of the body also showed profound changes. Individual fibers could be seen, twisted spirally and drawn together between other muscle fibers, which were still well preserved. The sarcolemma nuclei were much increased. The sarcolemma sheath was partly retracted from the contents; it also in many places showed irregular protrusions. The contractile protoplasm had been expelled in the shape of circumscribed, roundish masses which no longer showed any striation.

SUMMARY OF THE PATHOLOGY.

The following is a general outline of the special pathology of beriberi, summarized from a study of the literature on the subject and from that of a number of fatal cases examined by the author in Manila during the past three years:

The bodies of patients dead of beriberi generally promptly develop marked post-mortem rigor. However, in cases which succumb slowly to the atrophic type or in which complicating, wasting diseases, such as tuberculosis, amœbic dysentery, malaria, etc., are present, the post-mortem rigidity may be quite insignificant; this, however, is the exception and not the rule. When death has occurred very rapidly, as in the acute pernicious variety, the author has observed the post-mortem rigor develop very early and to become as strong as that met with in fulminating cases of Asiatic cholera or bubonic plague. According to M. Miura, post-mortem rigidity generally shows itself in beriberi within two hours after death, reaching its maximum within five or six hours post-mortem and lasting for a considerable period of time. The skin of the corpse is pale, with cyanotic patches scattered here and there. Occasionally cutaneous hemorrhages may be observed. On section the superficial veins discharge a large amount of dark, fluid blood and in the majority of cases, excepting only those of the atrophic variety or of long standing, the subcutaneous tissue is œdematous and exudes a considerable amount of serous fluid. The subcutaneous œdema is usually best marked at the anterior thoracic region and over the anterior surfaces of the lower extremities. Hydropericardium, ascites, and hydrothorax are very frequently encountered in beriberi autopsies. Hydropericardium is the most common of these serous effusions. The average of the post-mortem figures given by Scheube, Lodewjik-Weiss, Pekelharing and Winkler, and Yamagiwa, in a total of 256 cases, shows 66 per cent of hydropericardium. The author has likewise found hydropericardium in the majority of his autopsies on cases of this disease. Subepicardial and subpleural petechiæ are also not infrequently encountered.

The heart, of all the internal organs in beriberi, most constantly shows very characteristic changes. The myocardium, as a whole, is hypertrophic, and the hypertrophy is usually most marked in the right ventricle; but the left one may likewise be enlarged. The organ is then increased in size in all of its diameters and in its weight. The average of

the latter in 93 cases of beriberi reported by Yamagiwa was 368 grams, whereas the normal Japanese heart weighs from 250 to 300 grams. The right ventricle was hypertrophic in 73 of these 93 cases, the average diameter being 6.1 mm., compared with a normal diameter of 2 to 3 mm. The right ventricle, in particular, is generally not only hypertrophic but also markedly dilated, so that there is present a relative insufficiency of the tricuspid valve. All of the chambers generally contain a large amount of dark, fluid blood. Chicken-fat clots are also generally found in the heart in atrophic cases in which the death struggle has been protracted. The coronary veins are much dilated. The myocardium may be normal, but often it is found to be more or less cloudy and mottled, in consequence of diffuse, fatty degeneration.

As a rule, the lungs are œdematous, congested, and contain little air; however, occasionally they are emphysematous, and we have also seen some cases in which they were exceptionally collapsed and dry. At times, some catarrhal bronchitis may be observed and in some cases, where the pneumogastric has been profoundly affected, aspiration pneumonia has been seen. In beriberi the spleen shows no changes characteristic for this disease. It is true that in the Tropics a considerable enlargement has frequently been observed in beriberi; but this must be looked upon as a mere coincidence, because one must not forget that in tropical post-mortem material, no matter what the immediate cause of death has been, enlargement of the spleen is very frequently found. However, in beriberi this organ often shows cyanotic induration of a moderate degree. The kidneys, in acute cases, are markedly congested, and some cloudy swelling and fatty degeneration are frequently observable. The liver is generally swollen and congested. Where chronic passive congestion has lasted for some time, on section we find the characteristic appearance of a nutmeg liver.

In many cases of beriberi, particularly those of the subacute variety which have not lasted too long, we find great hyperæmia of the gastric and duodenal mucosa. Occasionally, ecchymoses are even found in the mucous membrane of this organ. Ellis [37] reports that he found the lining membrane of the stomach congested in 31 out of 57 fatal cases of beriberi, and in most of these it was intensely congested, especially on the ridges of the corrugations. In four instances there were blood clots present in the stomach, possibly due to the persistent vomiting from which the patient had suffered prior to death. This condition of the gastric and duodenal mucosa has so impressed several observers that they hold the stomach and duodenum to be the portal of entrance of the specific virus of beriberi. We have, like others, observed this hyperæmia in most of our necropsy cases; but we are inclined to

[37] Ellis: Contribution to the Pathology of Beriberi. *London Lancet* (1898), 2, 985.

look upon it as a purely mechanical, passive process due to general venous congestion, which often finds so marked an expression in the condition of the liver. The small intestine, excepting the duodenum, and the large intestine show no particular changes in beriberi.

The peripheral nerves, particularly those of the lower extremities, are almost without exception profoundly affected in this disease, but the changes are rarely noticeable to the naked eye. The changes found on microscopical examination clearly indicate that the most characteristic anatomical morbid process in beriberi is the degeneration of the peripheral nerves. This observation was first made by Baelz, Scheube, Miura, and Yamagiwa, and has later been confirmed by a considerable number of observers, including Pekelharing and Winkler, Wright and Duerck.

Summary of the histopathological changes.—In summarizing the histopathological changes the following lesions should be emphasized: The myocardium usually shows a more or less incomplete loss of the striation of its fibers. The latter are finely vacuolated, although larger vacuoles are also occasionally seen. Fragmentation and segmentation are generally present but it is not justifiable to attach as great a significance to these lesions in beriberi as Glogner has recently done, because they are so frequently found in a variety of diseases that they are not of specific importance. Among the changes in the myocardium must also be mentioned an occasional increase in the interstitial connective tissue. The lungs show no characteristic histological changes, but, in cases where there has been much congestion and œdema, dilated and densely filled interalveolar capillaries are present and the alveoli themselves contain a granular or coagulated, homogeneous material. Occasionally there is an increase of the interalveolar, the perivascular, and the peribronchial connective tissue. The spleen shows no characteristic changes, but an increase in the connective tissue, more or less endothelial proliferation and crowding of the pulp spaces with blood elements are frequently encountered. In the kidneys, as emphasized by Yamagiwa, are usually found cloudy swelling and fatty degeneration of the tubular epithelia. In uncomplicated cases, these parenchymatous changes are usually of a moderate degree. In the liver there is a great congestion of the intralobular capillaries, with fatty degeneration and cloudy swelling and even complete necrosis of the parenchyma cells. A change in the liver, to which Plehn has recently attached considerable importance, we have met with almost without exception. It consists of interlobular, inflammatory foci, composed of small, round cells which infiltrate the interlobular fibrous connective tissue. In fact, Plehn speaks of an interstitial hepatitis in beriberi. The mucosa of the stomach and duodenum exhibits dilated and congested vessels and in a number of cases a profound eosinophilia has been present. In the cases in which the eosinophiles were increased the presence of uncinaria could be excluded, and it is possible that this eosinophilia may have a certain significance in beriberi.

The most characteristic histological changes in beriberi are found in the peripheral nerves. Here, a degeneration of the myelin sheath occurs which varies from insignificant alterations to the most profound lesions. The myelin sheath is broken up into balls and beads, becomes gradually honeycombed and finally entirely disappears. Where it is profoundly altered, the axis cylinders likewise show distortion, irregular outlines, coiling up, or complete disappearance. These changes have been so completely described on a number of occasions and particularly by Yamagiwa and recently by Duerck, that it is not considered necessary here to give any further description of them. A proliferation of the neurolemma nuclei is generally associated with the degenerative changes in the myelin sheath and the axis cylinder. However, I have never found any changes of an inflammatory nature and agree with those who think that the morbid processes in the peripheral nerves in beriberi are purely degenerative in character. I have seen the profound degenerations in the peripheral nerves from very acute cases which Duerck has described. This seems to point to the fact that the poison of beriberi, whatever it may be, accumulates in the body and then leads to a sudden explosion. It is clear that such fundamental alterations in the nerves as are seen in acute, pernicious cases, can not have been produced during the few hours or days in which the disease apparently has continued, it is more probable that they are due to an agent which has accumulated during a certain period of time without leading to any manifest symptoms. In the more chronic cases, degenerative changes are also seen in the muscles supplied by the peripheral nerves and in these instances the voluntary muscle fibers are found with indistinct outlines and striation, and the sarcoplasm is either homogeneously swollen or shrunken away from the sarcolemma.

Rumpfe and Luce and Wright have also described degenerative changes in the axis cylinders and nerves of the cord and the latter mentions alterations in the ganglion cells of the spinal ganglia.

POST-MORTEM RECORDS AND HISTOLOGICAL STUDIES OF A NUMBER OF CASES OF BERIBERI.

The following post-mortem and histological studies of a number of cases are included for the purpose of illustrating the pathological types of the disease:

Case No. 1.—Acute pernicious beriberi with advanced degeneration of peripheral nerves.—Necropsy No. 1547, November 24, 1905: Lope Jacob, a Filipino prisoner in Bilibid penitentiary, had been working in the prison during November, 1905. As far as was known he had not been recently ill. During the night of November 23 he was attacked with palpitation of the heart, shortness of breath, weakness, and anxiety. At 1 a. m. his condition became so alarming that he was taken to the prison hospital. Here he rapidly failed and died at 5.25 a. m.

AUTOPSY five hours after death: Body of native about 20 to 25 years old. Rather strong, heavy set; normal development; cutaneous surface slightly œdematous; slight pitting on pressure over tibial region; rigor mortis moderate in upper extremities; very marked in lower ones and jaws. On section, the fat and the subcutaneous tissue are found to be moderately oedematous. Muscles very moist and of a pale-pink color. Superficial veins discharge much dark, fluid blood. The peritoneal cavity contains 650 cubic centimeters of a clear, amber-colored fluid. The diaphragm reaches to the lower border of fourth rib. Pericardial fluid considerably increased. *Heart* contains a large amount of dark fluid blood, also chicken-fat clots. On the anterior surface of the right ventricle are seen a number of small, confluent, subepicardial petechiæ; right auriculo-ventricular opening easily admits four fingers; right side much dilated; myocardium of right side moderately hypertrophied; pockets of pulmonary valves deep; left ventricle slightly hypertrophied; myocardium of fair consistency, of a general pink color with here and there a slight yellow mottling; valves in general normal. Endocardium smooth; at the beginning of the aorta a few atheromatous spots; coronary arteries normal; weight, 305 grams. *Lungs* collapsed; poor in air; grayish-pink in color with some purplish-blue spots on posterior surface of lower lobes. Pleuræ smooth; no adhesions. Lungs on section, dry; poor in blood; bronchial glands not enlarged; bronchial mucosa normal. Larynx normal; tonsils hypertrophied and congested; crypts deep and ragged. *Spleen*, tense, capsule transparent except over a small, circumscribed, opaque and thickened patch in the middle of the posterior border. On section, of a dark, chocolate-brown color and congested; pulp of good consistency; trabeculæ and follicles both distinct; follicles enlarged; weight, 365 grams. *Kidneys:* perirenal fat œdematous; both kidneys normal in size; capsules smooth; color, pinkish-gray; consistency increased; on section, congestion of a moderate degree is seen, the surface is dull, slightly yellowish, pelves smooth, relation of cortex to medulla, normal. Ureters, normal. Suprarenals, normal in size, deeply pigmented. *Bladder* contracted, mucous membrane pale. Prostate small and normal. *Stomach and duodenum* normal in outline and size, mucosa quite markedly hyperæmic; pancreas normal. *Liver* swollen, capsule transparent, purplish-blue with yellowish mottling, lobules indistinct, congested; gall bladder and bile ducts normal. *Intestines:* serosa pale and shining; wall of entire tract is œdematous. Mucosa of small intestine, except that of duodenum, pale; that of large intestine, swollen and hyperæmic, the hyperæmia not being uniform but generally present as small, irregular patches at the apices of the folds, and particularly well marked at the ileo-cæcal valve. *Brain:* weight 1,375 grams; dura adherent, thickened and opaque. Pacchionian granulations large; fluid in ventricles normal; brain tissue slightly hyperæmic, otherwise normal. Peripheral nerves, pneumogastic, obturator (crural branch), and popliteal have a normal appearance.

ANATOMICAL DIAGNOSIS.—*Hydropericardium, dilatation and moderate hypertrophy of the right, moderate hypertrophy of the left ventricle, moderate fatty degeneration of the myocardium, subepicardial petechiæ, enlargement and congestion of the spleen, congestion, fatty and parenchymatous degenerations of the kidneys and liver, marked hyperæmia of the gastric and duodenal mucosa, chronic catarrhal inflammation of the mucosa of the large intestine; ascites. General œdema of the subcutaneous connective tissue. Acute pernicious beriberi.*

MICROSCOPICAL EXAMINATION.—The fibers of the *myocardium* show a somewhat indistinct striation, the longitudinal striæ in particular are hazy and not sharp. The interstices between the fibers are rather wide; fragmentation and vacuolation are occasionally seen. *Kidneys:* the vessels of both cortex and medulla are moderately congested; glomeruli normal, but the lining epithelia of the convoluted tubules of the cortex generally show a marked degree of cloudy swelling.

Suprarenals: vessels highly congested, cells of the *zona fascicularis* highly vacuolated. *Liver:* the parenchyma cells show a moderate degree of fatty infiltration and degeneration. The interlobular connective tissue exhibits acute, inflammatory foci, composed of small, round cells. *Spleen* normal, pulp spaces densely filled with blood. Here and there one sees a pigmented malarial parasite; eosinophilic cells are very numerous throughout the sections. In the *stomach*, the *duodenum* and also in the *large intestine* the vessels of the mucosa are highly congested and the eosinophiles increased, but otherwise the organs are normal. The eosinophilic cells are found in largest numbers in the lower strata of the mucosa, next to the muscularis mucosa. Here are often seen from 30 to 60 eosinophilic leucocytes in one field, one-twelfth oil immersion, ocular No. 3; length of tube, 170 millimeters. The pancreas is normal. The tonsils are normal but in the recesses of the crypts there are found a large number of bacilli greatly resembling those of diphtheria. Sections from both the *crural* and the *popliteal nerves* show profound degenerative changes. The latter nerve is more markedly affected. Few intact myelin sheaths are visible. The remaining ones are nodular, beaded, fragmented, and in a state of complete, foamy or honeycombed degeneration. The axis cylinders are frequently irregular, shriveled, more or less twisted, or entirely absent. The neurolemma nuclei are moderately increased. Inflammatory changes are not present.

Case No. 2.—Acute pernicious beriberi.—Necropsy No. 1595, January 3, 1906: Jorge Madulid, 33 years old, a Filipino prisoner in Bilibid, suffered slight malaise for several days before his admission to the hospital at about 4 o'clock on the afternoon of January 2, 1906. At this time he was very ill, suffering with restlessness, shortness of breath, palpitation of the heart, and rapid and weak pulse. His symptoms increased in severity and he died at 9.45 p. m.

Autopsy January 3, 1906, fourteen hours after death: Body of a strong, well-nourished male Filipino about 30 to 40 years old. The skin at the dorsum of the feet and at the anterior surfaces over the tibiæ is slightly œdematous. Rigor mortis moderate. On section the superficial veins discharge a considerable amount of dark, fluid blood. The subcutaneous tissues are moderately œdematous, the muscles pale-pink and moderately moist. The abdominal cavity contains about 50 to 100 cubic centimeters of a clear, straw-colored fluid. The pericardium is considerably distended and contains 100 to 150 cubic centimeters of a liquid of the same color. The *heart* is enlarged, particularly the right ventricle. Here the myocardium measures from one-half to three-fourths of a centimeter in thickness. Both sides of the heart contain much dark, fluid blood besides chicken-fat clots. The auriculo-ventricular opening of the right side is considerably enlarged and easily admits four fingers. Both the pericardium and endocardium are smooth and the former shows a few, very small petechiæ. The myocardium as a whole is rather soft and flabby and of a pale-pink and grayish-yellow color. The heart weighs 340 grams. The *lungs* are heavy, the pleuræ smooth and transparent, showing quite a number of petechiæ and ecchymoses. On section, the lungs are dark, reddish-brown in color, highly congested, and very poor in air. The mucosa of the larynx, trachea and bronchi is somewhat swollen, hyperæmic and covered with a thin, foamy, slightly blood-tinged mucus. The *spleen* is considerably enlarged. The capsule is of a dull gray color, quite opaque, and here and there shows circumscribed areas of peri-splenetic thickening. The resistance of the organ is increased. On section, it is found to be dark, reddish-brown in color and very much congested. The trabeculæ are very distinct and quite noticeably widened. The pulp is highly congested. The *kidneys* are normal in size, grayish-pink in color on the surfaces and dull and somewhat grayish-yellow on the cut surface. Ureters, bladder, etc., are normal. The *liver* is somewhat swollen, its margins rounded, capsule smooth, transparent and dark, purplish-brown

in color. On section the organ discharges a large amount of dark, fluid blood and the surface presents to a moderate extent the picture of a nutmeg liver. The gall bladder contains a considerable quantity of dark, greenish-yellow bile, its walls are somewhat œdematous. The mucous membrane of the *stomach* and *duodenum* is moderately hyperæmic but does not show either petechiæ or ecchymoses. In general, the *intestines* are normal. Pancreas is normal. The *brain* is quite œdematous, somewhat hyperæmic, but otherwise normal. The peripheral nerves and skeletal muscles show no macroscopic changes.

ANATOMICAL DIAGNOSIS.—*Hypertrophy of the right ventricle, congestion and œdema of the lungs, enlargement, fibrosis and congestion of the spleen, marked parenchymatous degeneration of the kidneys, congestion of the liver, hydropericardium, ascites, slight general œdema of the subcutaneous tissues, œdema of the brain. Acute pernicious beriberi.*

MICROSCOPICAL EXAMINATION.—The myocardial fibers show a moderately clear striation; here and there may be distinctly seen the fine dust-like vacuolation of fatty degeneration and the coarse vacuoles of fatty infiltration. Occasionally, fragmented fibers are met with. The nuclei are generally sharp in outline and well stained. The interstitial connective tissue is slightly increased. In the pulmonary sections the vessels are all congested, particularly the inter-alveolar capillaries. There is some increase of connective tissue around the veins and arteries but the inter-alveolar connective tissue is not increased. Many of the alveoli contain granular material, desquamated epithelia, few leucocytes and a considerable number of erythrocytes; some alveoli are completely filled with blood. In the *spleen* the trabeculæ are widened and the connective tissue of the pulp is increased. A considerable proliferation of endothelial cells of the pulp spaces is discernible. The follicles are ill-defined. Malarial pigment or plasmodia are not found. In the *renal sections* considerable cloudy swelling of the epithelial cells is seen. In the *hepatic sections* the central areas of the lobules show complete fatty degeneration and even necrosis of the parenchyma cells. Between the lobules small, round celled subacute inflammatory foci are visible. The inner head of the *gastrocnemius* shows no minute changes, the striation of the fibres is very distinct, the nuclei well defined and well stained; in fact there are no signs of a degenerative process. The degenerative changes in the *peroneal nerve* and branches are moderate in degree but are characteristic. There is irregularity of the myelin sheath, swelling, rarefaction, and vacuolation.

Case No. 3.—Acute pernicious beriberi.—Necropsy No. 1619, January 20, 1906: Gregorio Flores, 26 years old, a Filipino prisoner in Bilibid, under a death sentence, was admitted January 18, 1906, to the prison hospital. He complained of weakness and shortness of breath. On admission at 8 a. m. his temperature was 36°.8 C.; pulse, 132; respiration, 32. During the afternoon the temperature rose to 37°.5 C. A urine examination on the morning of January 19 showed specific gravity 1,018, acid reaction; albumen present in small amount, some leucocytes and red-blood corpuscles. At 8 p. m. on January 19 the temperature was 38° C. At 8.20 p. m. the patient suddenly died.

AUTOPSY forty-eight hours after death: Body of a medium-sized, fairly well-nourished native. Post-mortem rigor well marked. Post-mortem lividity over the dependent parts of the body and around the neck. Skin somewhat cyanotic. On section, a considerable amount of a dark, fluid blood issues from the superficial veins. The muscular tissue is fairly moist and of a good pink color. The muscles of the calves are very soft and flabby. There is no marked œdema of the subcutaneous connective tissue. The abdominal cavity contains a small amount of clear fluid, but the pericardial fluid is markedly increased. *Heart:* The pericardium is normal. The epicardium, smooth; it shows a few small petechiæ. Myocardium somewhat hypertrophic, especially the right ventricle. Heart muscle

of fair consistency; somewhat grayish-pink but without any signs of marked fatty or parenchymatous degeneration. Coronaries, highly injected. Weight of heart, 315 grams. *Lungs:* the pleuræ are smooth. The anterior surfaces of the lungs are rather pale, purplish-pink; the posterior surfaces are dark purple. A few subpleural ecchymotic spots are noticeable. The lungs are inflated, very heavy and highly œdematous. The mucosa of the trachea and bronchi is somewhat swollen, highly œdematous, and the bronchial tree contains a considerable amount of a thin, somewhat blood-tinged, foamy liquid. *Larynx* normal, with the exception of hyperæmia of the mucosa, particularly of the epiglottis. Tonsils, uvula, etc., normal. *Spleen:* somewhat enlarged, firm in consistency; on section, dark brown-red. Trabeculæ, distinct; follicles, obscure. The *kidneys* are both distinctly small, the right one larger than the other. They are pinkish-gray in color; capsules smooth, peeling off easily. On section, their surfaces present moderately congested vessels. Relation of medulla to cortex, normal; tubules decidedly grayish-white; pyramids quite dark in consequence of vascular congestion. Pelves very small, the left one contains a few drops of a creamy, yellowish, purulent fluid. Ureters, normal. Prostate, normal. The *bladder* is small and almost as solid and muscular as a uterus. Its muscularis measures almost 1 centimeter in diameter, mucosa likewise thick, corrugated, somewhat hyperæmic, but otherwise normal. The organ contains a very small amount of turbid urine. The ureters and the testicles are normal, but the prepuce is long and its opening is not larger than a small pin head. The skin covering the glans penis resembles a delicate mucous membrane. The inner surface of the prepuce is covered with desquamated epithelium. The *liver* is normal in size, capsule smooth, external surface somewhat mottled. On section, interlobular vessels and capillaries much injected; rows of liver cells, pale gray. *Gall-bladder* wall quite œdematous. *Stomach* and *intestines:* normal except that the mucosa of the small intestine is very hyperæmic. *Brain:* normal; weight, 1,270 grams.

Anatomical diagnosis.—*Hydropericardium, moderate hypertrophy of the myocardium, subepicardial and subpleural petechiæ, enlargement and cyanotic induration of the spleen; parenchymatous nephritis, hypertrophy of the muscularis of the urinary bladder, congenital phimosis, moderate chronic passive congestion of the liver. Acute beriberi.*

Microscopical examination.—In the *myocardium* the striation of the cells is generally very indistinct and in places completely obliterated; fine vacuolation is frequently seen and fragmentation is very pronounced. There is also some increase in the interstitial connective tissue. In the *pulmonary sections* the most marked histological change is found in the alveoli, many of which are more or less completely filled either with a granular, or a homogeneous, coagulated material, (serious exudate, coagulated by the fixing process). Some of the air spaces also contain red blood corpuscles. The *spleen* shows considerable increase in connective tissue and some proliferation of the pulp endothelia. In the *renal tissue* the epithelia of the convoluted tubules generally show cloudy swelling. The intralobular capillaries of the *hepatic sections* are injected, the parenchyma cells in the central part of the lobule show fatty changes. The interlobular connective tissue exhibits some small, round-cell periportal inflammatory areas. In transverse sections of the wall of the *urinary bladder* it is found that the muscularis is not only very much thickened as a whole but that the individual muscle fibers are considerably hypertrophied, so that many measure in length from 200–250 μ. Sections of the gastrocnemius show no marked changes. The peripheral nerves (the popliteal and its branches), examined both in transverse and in longitudinal sections, show advanced degeneration of the myelin sheath, consisting of irregularities, "rosary swelling," and rarefaction. In places there is loss of the sheath.

Case No. 4.—Acute, pernicious beriberi.—Necropsy No. 1663, February 20, 1906: Andres Rabamontano; residence, 346 Cabildo; native Filipino, 18 years old; died quite suddenly at 11 a. m. February 19, 1906, without any previous illness.

AUTOPSY twenty-four hours after death: Body of a strong, muscular native. The post-mortem rigidity is still marked, but it is less strong in the upper than in the lower extremities. Post-mortem lividity well marked, particularly on the dependent parts and around the neck. The face is somewhat puffed, the thorax and sides markedly œdematous; however, there is no appreciable œdema of the lower extremities. On section, the superficial veins discharge a large amount of dark, fluid blood. The subcutaneous tissues of the thorax and, to a lesser extent, those of the abdominal walls are œdematous. The pericardium contains about 300 cubic centimeters, the abdominal cavity about 400–450 cubic centimeters of a clear, straw-colored, serous fluid. *Heart:* The myocardium is hypertrophic, the wall of the right ventricle has a diameter of about 0.6 centimeter, its walls are of a pink color with a few grayish-yellow spots. It weighs 340 grams. *Lungs:* congested, œdematous, increased in consistency, and on the cut surface rather dark brownish-red in color. *Spleen:* capsule very tense, grayish-reddish-purple color; cut surface, brown-red; pulp, rather firm, does not protrude; follicles and trabeculæ, distinct. *Kidneys* and *liver:* much congested, somewhat increased in consistency, otherwise normal. Gall-bladder wall, highly œdematous; its mucosa swollen. Gastric and duodenal mucosa, moderately hyperæmic. Otherwise all internal organs normal. *Nerves* and skeletal muscles show no macroscopic changes.

ANATOMICAL DIAGNOSIS.—*Hydropericardium, hypertrophy of the myocardium, œdema, congestion and cyanotic induration of the lungs, congestion of the spleen, kidneys, and liver, ascites, œdema of the subcutaneous connective tissue. Acute pernicious beriberi.*

MICROSCOPICAL EXAMINATION shows fragmentation of the *myocardium* (otherwise the fibers are perfectly normal), cloudy swelling and fatty degeneration of liver parenchyma cells; and subacute interlobular inflammatory foci. The *popliteal* and *peroneal nerves* show a minor degree of degeneration of the myelin sheath. (The nerves in this very acute pernicious case were removed, handled, and fixed with great care, so that the changes noticed are not due to artefacts.)

Case No. 5.—Acute, wet beriberi with splenomegaly.—Necropsy No. 1225, January 28, 1905: Examination seventeen hours after death in Bilibid Prison morgue of the body of Placido Bajian, Visayan, 34 years old. The patient had been previously working with a gang of prisoners at Fort McKinley. A few days before his death he had been returned on account of sickness to the prison hospital. *Clinical diagnosis: Wet beriberi. Pulmonary œdema.*

AUTOPSY.—Body of a strong, well-nourished native, post-mortem rigidity well marked; post-mortem lividity present over dependent parts. The skin over the entire body is slightly œdematous and pits on pressure. On section the subcutaneous tissue discharges a small amount of serous fluid. The muscles are quite pale and moist. Both the thoracic and abdominal cavities contain a few ounces of slightly cloudy, serous fluid. *Pericardium:* smooth, transparent, contains a somewhat increased amount of fluid. *Heart:* somewhat enlarged in all of its dimensions, epicardium, smooth and transparent, subepicardial fat very moderate in amount. Myocardium, soft and flabby. Both auriculo-ventricular openings enlarged in diameter; the cavities contain chicken-fat coagula and dark, fluid blood. *Endocardium:* smooth, all valves normal, no atheromatous spots in aorta. Color of myocardium, pale, pink, grayish-yellow, cut surface dull. Weight of heart, 325 grams. *Lungs:* pleural surfaces, smooth, few old fibrous adhesions on the lower lobe of the left side; when inflated, pale-grayish-pink except the posterior surfaces

of the lower lobes, which are purplish-blue; in general they contain much serous fluid, the lower lobes much dark blood. Bronchial and tracheal mucosa, smooth and pale. Bronchial glands not enlarged. Spleen very large, weight 910 grams, general configuration that of a normal spleen. Capsule, smooth, tense, not wrinkled; in general, transparent, except over the left half of the upper surface where it is nontransparent, grayish-white, considerably thickened. Pulp, moderately soft, dark brown-red, cut surface smooth. Trabeculæ, quite distinct, broadened; follicles, fairly distinct. *Kidneys* of normal size, capsules smooth, peel off easily. External color, bluish-purple; cut surface, dark, pinkish-purple; vessels, much injected; tubules of cortex grayish-white; pyramids rather pale. Relation of cortex to medulla, normal; pelves, normal; ureters and bladder, normal. Suprarenals, small, rather hard, dark-brown yellowish. *Liver:* large, greatly congested; externally purplish; on section, brownish-yellow; acini, distinct; interacinous connective tissue possibly somewhat increased. *Gall bladder* and *ducts:* normal. The former contains a considerable quantity of dark, greenish-yellow bile. *Pancreas:* normal. *Stomach* and *intestines:* normal, with the exception of considerable congestion of the gastric veins and a marked hyperæmia of the gastric mucosa. Intestinal mucosa in general pale, except that of the rectum, which is somewhat hyperæmic. No amœbic ulcerations. Scrotum much distended. The left side contains a hydrocele enclosing about 50 cubic centimeters of a straw-colored, serous fluid. On the right side, the testicle is surrounded by a fibrous mass about 0.6 to 1 centimeter in diameter. The fibrous tissue is very tough and is continuous with the tunica albuginea. The testicle contained in this fibrous mass is small, but appears otherwise normal and not atrophic. *Brain:* the dura mater is quite tense, amount of cerebro-spinal fluid, large; brain pale but œdematous, ventricles contain an increased amount of fluid. Otherwise the brain is normal. Weight, 1,335 grams.

ANATOMICAL DIAGNOSIS.—*Moderate hypertrophy, dilatation and fatty degeneration of the myocardium, œdema of the lungs, splenomegaly and perisplenitis, congestion of the liver, hydrocele of the left side, chronic fibrosis of the right tunica albuginea, general anæmia, general, moderate œdema. Chronic or subacute, wet beriberi.*

Smears from the spleen show neither malarial parasites nor the Leishman-Donovan bodies.

MICROSCOPICAL EXAMINATION.—*Myocardium* striation quite distinct, no well-marked evidences of fatty degeneration; fragmentation and segmentation pronounced. *Lungs:* inter-alveolar septa broadened, many alveoli contain considerable granular and coagulated serous material. There is marked vascular congestion. *Kidneys:* considerable cloudy swelling of uriniferous epithelia. *Spleen:* much increase in connective tissue, particularly of the trabeculæ; very little, if any, endothelial proliferation; crowding of the pulp spaces with blood elements; moderate amount of pigment, no malarial parasites or Leishman-Donovan bodies. The liver in this case, aside from great congestion, fatty degeneration of parenchyma cells, and a moderate amount of pigment, shows subacute interlobular periportal inflammatory foci. The other organs examined (the stomach, pancreas, suprarenals, testicles) show nothing abnormal. The popliteal nerve and branches show the typical degenerative changes of the myelin sheath and axis cylinders.

Case No. 6.—Acute, wet, beriberi complicated by malaria.—Necropsy No. 1190, May 23, 1905: Eustaquio Alvarez, a prisoner of Bilibid, 28 years old, native Visayan, was suddenly taken seriously ill on May 21, 1905, and was admitted to the hospital during the night of May 22, with a temperature of 37°.5. The following morning at 8 o'clock his temperature was 36°.9. He complained of shortness of breath and weakness. On examination the pulse was weak, soft,

easily compressible, and 100 beats per minute. After the patient had walked about the room for a short time it increased to 141. The heart's area of dullness was increased downwardly and to the right, and a systolic bruit could best be heard at the base of the organ. The lower extremities were somewhat œdematous, the skin pitting slightly on pressure. There was no pain complained of in the calves. The patellar reflex on the left side was normal, that on the right accentuated. On May 22 the condition of the patient became worse, the difficulty in respiration increased, and the temperature at 8 o'clock in the evening had risen to 39°. He died at 2.30 a. m. on the next day.

AUTOPSY, eight hours after death. Body of a strong, well-nourished native, no deformities, medium weight, apparent age 25 to 30 years. Post-mortem rigidity very marked, involving extremities, jaws and the muscles in general. Post-mortem lividity present in the dependent parts of the body. The lymphatic glands are not palpable. On section, the superficial vessels discharge a considerable amount of dark, fluid blood and the subcutaneous connective tissue is found to be œdematous; the muscles are quite moist. The pleural cavity contains a few ounces of clear, straw-colored serum. Both pleuræ show a number of petechiæ. The *lungs* in general form are normal and of pinkish-gray color. They are inflated. On section, the blood vessels are found to be congested and a large amount of watery fluid can be pressed out of the tissues. The trachea and bronchi are normal but the epiglottis shows a few petechiæ. *Heart:* the pericardium contains a somewhat increased amount of clear, serous fluid. The myocardium exhibits a few spots of subepicardial hæmorrhages; it is of normal consistency. The right side is considerably dilated, markedly hypertrophied, and the whole heart weighs 360 grams. It contains dark, fluid blood and gelatinous clots. The muscle is pink in color, with a few grayish-yellow spots. The coronary vessels are tortuous and distended. The abdominal cavity contains about 300 cubic centimeters of straw-colored, clear fluid. The mesenteric and post-peritoneal glands are not enlarged. The *spleen* weighs 540 grams. It is very soft, dark grayish-purple externally and on section dark brownish-black. The pulp is very soft and protrudes over the surface. The trabeculæ and the Malpighian bodies are not distinct. The *liver* is normal in size, somewhat increased in consistency, surface smooth, externally reddish-brown. On section its vessels discharge a considerable quantity of dark, fluid blood. The gall bladder, which contains about two to three dozen small, very dark stones, is normal except that its walls are very œdamatous. The *kidneys* are normal in size, their surface is smooth, dark grayish-pink in appearance, consistency rather soft, capsules peel off easily. On section the vessels appear moderately congested, the surface is rather dull, tubules grayish-white. Ureters, bladder, pancreas, etc., normal. The stomach and the intestines show nothing abnormal. Their mucosa is rather pale-gray as far as the stomach is concerned, but hyperæmic in the small and large intestines. The *brain* is normal but quite œdematous. The ventricles contain about 30 to 50 cubic centimeters of clear fluid. The peripheral *nerves* show no changes.

ANATOMICAL DIAGNOSIS.—*Dilatation of the right side of the heart, moderate general hypertrophy of the myocardium, œdema of the lungs and of the brain, moderate general anasarca, acute, parenchymatous nephritis, congestion of the liver, colelithiasis, enlargement, pigmentation, and softening of the spleen. Acute, wet beriberi (complicated, as shown by the microscopical examination, with æstivo-autumnal malaria).*

MICROSCOPICAL EXAMINATION.—*Myocardium:* the fibers, aside from fragmentation, show no changes. The nuclei are well stained and clear cut. Striation of the sarcoplasm is very distinct. In the lungs, the blood vessels are dilated

and congested. Here and there the connective tissue of the intra-alveolar septa is increased. Many of the alveoli contain desquamated cells and granular detritus. In the *spleen* the pulp spaces are much crowded with red blood corpuscles, among which are a moderate number of leucocytes. The follicles are not sharply defined, the trabeculæ are thin, the connective tissue in general is not increased. Both in the pulp spaces and in the follicles a considerable amount of extra- and intracellular dark-brown pigment is encountered. Parasites of æstivo-autumnal malaria are fairly numerous. In the *liver*, the interlobular capillaries are dilated and filled with blood. The parenchyma cells show some fatty and well-marked cloudy changes. The most prominent histologic deviation from the normal type is found in the interlobular connective tissue. Here we see a periportal inflammatory infiltration composed of small, round lymphoid cells, some ordinary polynuclear and quite a few eosinophilic cells. Fine, dark, pigment granules are seen all through the hepatic sections while the interlobular foci also show coarser pigment granules. In these foci malarial parasites are likewise encountered. The renal sections show cloudy swelling of the tubular epithelia, with much granular material; otherwise there are no marked changes. In the *stomach*, the mucosa, which is otherwise normal, shows a moderate eosinophilia. In the mucosa of the *small intestine* very large numbers of polynuclear eosinophiles are present. These cells are found throughout the mucosa; they extend into the muscularis mucosæ and into the surrounding, loose connective tissue. The popliteal nerve and its branches show but a very moderate degree of degeneration of the myelin sheath, but some is undoubtedly present.

Case No. 7.—Acute beriberi complicated by malaria.—Necropsy No. 1674, March 7, 1906: Post-mortem examination at St. Paul's Hospital on the body of Okumura Kakuzo, a Japanese, 18 to 20 years old. This man had been under observation while sick at the hospital for two or three days. Absence of the patellar reflex, paresis of the lower extremities and dyspnoea had been noted. A blood examination showed malarial parasites of the æstivo-autumnal type. A few ova of *uncinaria duodenale* were found upon examination of the stools. *Clinical diagnosis, beriberi complicated by malaria.* The patient died March 6 at 8.30 p. m.

Autopsy.—Twenty hours after death: The body is that of a well-developed, rather strong Japanese, well nourished, no anomalies. The anterior tibial surfaces of the legs show a few, shallow cicatrices. *Rigor mortis*, well marked. Posterior surface of the body shows extensive areas of lividity. The important lesions observed may be summarized as follows: The pericardial fluid is increased, the *heart* is hypertrophied, and the wall of the right ventricle has a thickness of from 6 to 8 millimeters. The consistency of the myocardium is normal; the color is pink, with a few yellowish spots. The *lungs* are œdematous, but otherwise normal. The *spleen* weighs about 450 grams. It is dark, purplish-gray externally, and on section, of a light-reddish-brown color. The pulp is very soft and protrudes over the cut surface. Follicles and trabeculæ are not easily distinguished. The *liver* is large, swollen, grayish-pink in color with numerous yellow dots. On the cut surface it is dull grayish-pink and the veins discharge a considerable quantity of blood. The kidneys are normal in size, the capsules peel off easily, and the cut surface shows a peculiar rose or pink color. The mucosa of the stomach and duodenum is moderately hyperæmic. Otherwise the internal organs are normal. No uncinaria are found in the small intestine.

Anatomical diagnosis.—*Moderate hydropericardium, hypertrophy of the myocardium, œdema of the lungs, enlargement, congestion and softening of the spleen, hyperæmia of the kidneys, congestion, fatty and parenchymatous degeneration of the liver, hyperæmia of the gastric and duodenal mucosa, acute pernicious beriberi.*

During the post-mortem examination, two agar tubes were inoculated from the cerebro-spinal fluid obtained by puncture with a sterile syringe at the third lumbar vertebrae. Another tube was inoculated from the heart's blood and pieces of the wall of the stomach and of the duodenum with some gastric contents were placed in a flask containing several hundred cubic centimeters of alkaline bouillon. The bouillon was then heated to 80° C. and kept at that temperature for about ten minutes. It was then cooled in the refrigerator and subsequently incubated. (Experiments with these cultures are reported above.)

MICROSCOPICAL EXAMINATION.—The *myocardial* fibers are a little hazy in striation and here and there finely vacuolated. Fragmentation is pronounced. The *splenic sections* show some increase in connective tissue, considerable endothelial proliferation, and pigment, and a number of malarial parasites. Pigment and malarial parasites are also found in the *liver sections* which also show somewhat extensive acute inflammatory interlobular foci. There is some granular degeneration of the parenchyma cells. The sections from the *stomach* and *duodenum* show nothing abnormal. Those of the nerves reveal advanced degenerative changes.

Case No. 8.—Subacute, wet beriberi.—Necropsy No. 913, March 7, 1904 (history kindly furnished by Dr. G. B. Cook): Antonio Ybalio, a Filipino, policeman, 36 years old. *Previous history:* Patient was ill in Civil Hospital from January 17 to 30, 1904, and was treated for amœbic dysentery. At this time he complained of insomnia, pain in the abdomen, slight cough, and moderate fever (37°.7). There was no anasarca present. Amœbæ and ova of *Trichocephalus dispar* were found in his stools on January 18. Treatment with quinine enemata was instituted, under which he improved, leaving the hospital on January 30, 1904. The report of the stool examination at this time was negative for amœbæ. *Present illness:* On February 28, 1904, he again entered the hospital stating that he had not been well since his illness in January, but during this time had become weaker and weaker, swelling of his legs had developed, and he had suffered, in addition, with pain in the abdomen, anorexia, dyspnœa, insomnia, difficulty in locomotion, and constipation. His temperature was subnormal throughout his present illness until just before he died, when it registered 37.7°. *Physical examination:* Expression heavy, face swollen, respiration labored; general anasarca especially marked in feet and legs; abdomen, distended and painful on pressure. Pain was elicited on pressure over tibiæ. Apex beat, forcible and displaced to left of normal position about 2 to 2.5 centimeters. A double murmur of a blowing character could be heard most distinctly at the apex. The reflexes were not tested. *Course of illness and treatment:* On admission he was given Liq. potass. arsen. *gtts.* 6 three times daily, nourishing diet, and a cathartic of magnesium sulphate when necessary. On March 1 the urine examination was as follows: Specific gravity, 1,023; acid; small amount of albumen; urea, 26.46 grams per liter; sediment slight, very many hyaline and a few granular casts. After receipt of this report the diet was restricted; Fowler's solution omitted and infusion of digitalis and lithium citrate given. His condition steadily grew worse and he died on March 6, 1904, at 11.30 p. m.

AUTOPSY fourteen hours after death: Body of a well-developed Filipino, about 35 to 40 years old. Post-mortem rigidity and lividity well marked. The integument is quite œdematous, particularly over the abdomen, the anterior surface of the legs and at the dorsum of the feet, where the skin pits on pressure. The scrotum is œdematous and swollen to about two to three times its normal size. On both legs and forearms small, symmetrically placed pinhead sized petechiæ are visible The scleræ are somewhat icteric. On section, the veins discharge a considerable amount of dark, fluid blood. The subcutaneous

connective tissue is œdematous, in places even gelatinous. On opening the spinal canal and the cranial cavity, the dura is found to be tense, the amount of cerebro-spinal fluid increased. The vessels of the pia-arachnoid are injected, and the brain itself is rather œdematous; fluid in the ventricles is increased; otherwise, the brain and the cord are normal. The thoracic as well as the abdominal cavity contains a moderate amount of clear, straw-colored fluid. *Pericardium:* smooth, glistening, translucent, distended by an increased amount of clear, serous fluid; probably three to four times as much as normally found. The *heart* is large, soft, and flabby; dimensions, 16 centimeters from base to apex, 12 centimeters from side to side, 7.5 centimeters from before to backward. Visceral pericardium, smooth; coronary veins much injected, deep-bluish-purple in color; both auriculo-ventricular openings somewhat enlarged. Auriculo-ventricular valves on right side not quite competent. Endocardium, smooth except over the aortic valves. These are markedly thickened, somewhat nodular, and slightly retracted toward their peripheral attachment. However, there are neither loss of substance nor any adhesions. Beginning of aorta, atheromatous. *Lungs:* adherent by old fibrous adhesions, which are difficult to separate. Adhesions present at the apices as well as at the diaphragmatic surfaces. Purplish-gray in color at the upper lobes, quite deep purplish at the lower ones. On section, much blood and œdematous fluid escapes. The lower lobes in particular contain a considerable amount of dark, fluid blood and very little air. The bronchi contain frothy mucus. Mucous membranes of trachea and bronchi, somewhat injected and swollen. *Spleen:* 10 by 8 by 5 centimeters. Capsule, on the whole, smooth though slightly wrinkled; pinkish-red; on section, dark-brown. Trabeculæ, well-marked; pulp, fairly soft, somewhat protruding. *Kidneys:* 11.5 by 6 by 5 centimeters; pinkish-reddish-purple; after removal of capsules, which strip off easily, areas of a more grayish color are seen. On section, cortex 3 to 9 millimeters; vessels, injected; tubules, grayish-yellow; pyramids, dark brownish-red, much injected. Mucous membrane of pelves, smooth; suprarenals, swollen, enlarged, quite soft, dark-purple in color. *Liver:* rather small, pinkish-gray; capsule, smooth, translucent; center of lobules appear as rather pale, shiny grayish areas. On section, color is in general rather dark pink-purplish mixed with grayish-yellow. Vessels contain much dark blood. *Gall bladder:* distended with turbid, dark green bile; mucous membranes, smooth, no stones. *Pancreas:* large, rather soft; otherwise normal. *Stomach:* serosa smooth, shining, transparent; veins much injected, particularly those radiating from the lesser curvature; gastric mucosa thrown into prominent rugæ, much congested, of a pale, pink color with a hue of purple. Oesophageal mucosa, likewise, though more moderately, injected. *Intestines:* the serosa is markedly injected over the whole length; the process is more marked in the serosa of the small intestine. *Duodenum:* mucosa, somewhat swollen; vessels, injected, pinkish-red in color. The mucosa of the jejunum and ileum is likewise injected, though less than that of the duodenum. Peyer's patches distinctly swollen. Appendix, normal. Large intestines, practically normal except slight injection of the mucosa.

ANATOMICAL DIAGNOSIS.—*Hydropericardium, dilatation and hypertrophy of the myocardium, chronic endocarditis of the aortic valves, atheromatosis of the aorta, congestion and œdema of the lungs, hyperæmia of the gastric and intestinal mucosa, parenchymatous degeneration of the kidneys and liver, enlargement and chronic congestion of the spleen, hydrothorax, ascites, general œdema of the subcutaneous connective tissue. Subacute, wet beriberi.*

MICROSCOPICAL EXAMINATION.—*Myocardium:* striation of fibers in places completely lost; fine and coarse vacuolation; granular degeneration very pronounced;

fragmentation well marked in some places; many poorly stained nuclei. Pulmonary alveoli contain much granular material; interalveolar capillaris, distended and densely filled; peribronchial and perivascular connective tissue somewhat increased. *Spleen:* increase in connective tissue, considerable; proliferation of pulp endothelia. *Kidneys:* tubular epithelia show cloudy swelling of a moderate degree and extent. Here and there, granular material in tubules. Otherwise, no changes. The *liver* in some parts shows great congestion of intralobular capillaries with fatty and granular degeneration, necrosis of parenchyma cells and interlobular, subacute inflammatory foci; in other parts, an advanced necrosis and atrophy of parenchyma cells of the central areas of the lobules is seen. The *gastric* and *intestinal mucosa,* aside from vascular congestion, shows no marked changes. The *popliteal nerve* and branches show advanced degenerative changes and a marked increase in the neurolemma nuclei; however, no inflammatory changes of any kind are present.

Case No. 9.—Subacute, wet beriberi.—Necropsy No. 1536, November 17, 1905: Agaton Caber, 24 years old, male Filipino, prisoner at Bilibid, died November 16 at midnight.

AUTOPSY twelve hours after death: Body of a strong, young male Filipino. Post-mortem rigidity and lividity well marked. The whole surface of the body is œdematous; this is most marked at the lower extremities, where the skin pits on pressure. On section, the subcutaneous areolar tissue discharges a considerable amount of a clear, serous fluid. The muscles are moist and of a rather pale-pink color. The *pericardium* is smooth and shiny, tensely expanded, and contains an increased amount of clear, amber-colored pericardial fluid. The *heart* is moderately enlarged. There is hypertrophy with some dilitation of the right ventricle. Both sides contain chicken-fat clots; the tricuspid opening is somewhat enlarged. The endocardium and the epicardium are smooth and otherwise normal. The myocardium is of very fair consistency, dull-pale-pink in color. The heart weighs 340 grams. *Lungs:* The pleural sacs contain an increased amount of clear fluid; the pleuræ are smooth, they show a very few small, subpleural petechiæ. In general, the external color of the lungs is of a pink-purple, except on the posterior surface of the lower lobes, where the color is a deep bluish-purple. The lower lobes, on section, discharge much dark blood; the upper ones are very œdematous. The pulmonary tissue is comparatively poor in air. The bronchial glands are normal, the bronchi contain a considerable amount of a thin, foamy fluid. The *spleen* is enlarged to about twice its normal size; capsule, of a steel-blue color, very tense. The pulp protrudes slightly on section. It is moderately soft, and much congested; trabeculæ, enlarged; follicles, fairly well visible; color, dark-brown. *Kidneys,* normal in size; capsules, smooth, pink-purplish with grayish-yellow mottling. On section, tubules grayish-white, vessels moderately injected; relation of medulla to cortex, normal; pelves, normal, capsules peel off easily; suprarenals, small, œdematous, quite intensely pigmented; bladder, etc., normal. *Stomach* and *duodenum,* serosa slightly hyperæmic; mucosa, markedly so, otherwise nothing abnormal. *Jejunum* and *ileum,* serosa and mucosa hyperæmic, intestinal wall as a whole somewhat œdematous. Large intestine, normal. The peritoneal cavity contains a considerable amount of clear, straw-colored fluid. The *liver* is somewhat swollen; capsule, smooth, tense, dark-purplish-blue. On section, liver lobules indistinct, yellowish mottling. Vessels discharge much dark fluid blood. Brain, œdematous, otherwise normal. Weight, 1,385 grams.

ANATOMICAL DIAGNOSIS.—*Moderate hypertrophy of the right side of the heart, œdema of the lungs, moderate fatty degeneration of the kidney and liver, enlargement of the spleen, hyperæmia of the gastric and intestinal mucosa, œdema of the brain, general moderate anasarca. Subacute, wet beriberi.*

MICROSCOPICAL EXAMINATION.—The *myocardial* fibers show a fairly distinct striation and some fine, dust-like vacuolation. Nuclei, well stained, fragmentation present to a moderate extent, interstitial connective tissue somewhat increased. The pulmonary interalveolar capillaries and the vessels of the *lungs* in general are congested; the alveoli partly filled with a cellular and serous exudate; the peribronchial connective tissue here and there somewhat increased. In the *spleen* the connective tissue is much increased and the pulp spaces are crowded with blood cells; outlines of follicles, indistinct. The tubular epithelia of the kidneys show cloudy swelling and fatty degeneration, but in general only in moderate degree. The *hepatic sections* show congestion of the intralobular capillaries, fatty degeneration of the cells in the center of the lobule and interlobular, periportal, subacute, inflammatory foci. A pronounced eosinophilia is found in the mucosa of the stomach and of the duodenum. The degenerative changes in the popliteal nerve and its branches are well advanced.

Case No. 10.—Subacute beriberi complicated with malaria and amœbiasis.—Necropsy No. 1636, February 1, 1906 (history kindly furnished by Dr. G. B. Cook). Donoso Coronel, a native Filipino of 45 years, light-house keeper in Manila Bay, assumed the duties of his position some time in December, 1905. Seven days after going to work in the light-house (according to the statements of the patient, who appears to be quite dull mentally) he became sick, but remained in the light-house for three more weeks, when he finally entered the Civil Hospital. On admission, patient could not walk on account of partial paralysis of the legs; his expression was heavy and he complained of pain in the abdomen; lower eyelids, puffy, and lower extremities, œdematous, pitting on pressure. Pulse, 114, apex beat displaced outward and downward, the second sound at the apex is prolonged and the second pulmonic sound is accentuated. There is visible pulsation in the upper epigastric region. The patient complains of pain in the abdomen and in the muscles of the legs and forearms. There is decided pain on pressure of the calves. The legs are moved slowly and with difficulty, extension of the feet and legs is weak; there is no ankle or wrist drop; the patellar reflexes are absent. On admission, the temperature registered 38.5°. Æstivo-autumnal malarial parasites were found in the blood and amœbæ in the stools. On January 26 the patient was examined by the writer, who found all of the more typical symptoms of subacute, wet beriberi. Some of the blood of the patient was drawn from the median cephalic vein and used for incubation and for animal experiments (reported above). The patient died February 1, 1906, at 4.20 a. m.

AUTOPSY four hours after death: Native Filipino of medium size and good nutrition. Post-mortem rigidity marked; post-mortem lividity, beginning to show on dependent portions of the body. The dorsum of the feet and of the legs is slightly œdematous. On section, the superficial veins discharge a considerable amount of dark, fluid blood. The subcutaneous connective tissue is slightly œdematous. The pericardium contains about 100 cubic centimeters of a clear, straw-colored serum; the pleural and the abdominal cavities, each several hundred cubic centimeters. The *heart* is considerably enlarged in all of its dimensions. The right auriculo-ventricular opening admits five fingers; the myocardial wall of the right ventricle measures 6 to 7 millimeters in thickness. The left auriculo-ventricular opening admits three fingers, and the myocardium of the left side is likewise hypertrophic. Epicardium and endocardium, smooth and otherwise normal. Myocardium of fair consistency, but pale yellowish-gray. Papillary muscle of left side considerably hypertrophied. *Lungs:* collapsed, poor in air, bound down by some old, fibrous adhesions; externally, grayish-pink with some purple in the lower and posterior parts. They are found to be rather dry on section. The bronchi contain a rather thick, foamy liquid; the mucosa is pale and not swollen; the bronchial glands are normal. The *spleen* is enlarged to

about twice the normal size; it is soft, intensely congested, dark brownish-black; follicles and trabeculæ, distinct. The *kidneys* are normal in size, rather firm in consistency, pinkish-gray externally; capsules, smooth, peel off easily. On section, tubules, grayish-white, slightly cloudy; vessels, congested; pelves, normal; ureters, bladder, etc., normal. The *mucosa of the stomach* is slightly hyperæmic at the apices of the folds; that of the duodenum is likewise hyperæmic. The ducts of the gall bladder are open. *Liver:* swollen, tense, grayish-dark in color; on section, brownish-yellow. The mucosa of the *rectum* and *colon* is hyperæmic and shows a few shallow ulcerations; otherwise, normal.

ANATOMICAL DIAGNOSIS.—*Hydropericardium, hydrothorax, ascites, hypertrophy of the myocardium and dilatation of the right heart; congestion, hypertrophy and pigmentation of the spleen, parenchymatous degeneration of the kidneys and liver. Hyperæmia of the gastric and duodenal mucosa; amœbic ulcerations of the large intestines. Subacute, wet beriberi.*

MICROSCOPICAL EXAMINATION.—The *myocardium* shows an indistinct striation, fine, with a coarser vacuolation here and there, fragmentation and segmentation and some increase in connective tissue. The pulmonary sections show no pronounced changes. In the *spleen*, a considerable amount of pigment and a moderate number of malarial parasites are seen. The *renal* sections exhibit considerable cloudy swelling of the uriniferous tubules. In the liver there is found congestion of the intralobular capillaries, cloudy swelling and fatty degeneration of parenchyma cells and interlobular, periportal, subacute, inflammatory foci. The stomach and the duodenum do not show any particular changes. In the large intestine there are erosions and ulcerations with leucocytic infiltration of the mucosa. Amœbæ, however, were not discovered in the sections examined. The degeneration of the peripheral nerves is very pronounced, there are irregularities, beaded swellings, honeycombing, and sometimes a complete loss of the myelin sheath.

Case No. 11.—Chronic, dry beriberi.—Necropsy No. 1617, January 19, 1906: Evaristo Rivera, a 35-year-old Filipino, a prisoner at Bilibid, was admitted to the hospital on January 5, 1906. He had been suffering for some time from indefinite symptoms and from muscular pains with some disturbances of motion. His case was first diagnosed as muscular rheumatism. Later on, absence of patellar reflex, enlargement of the heart toward the right side and other symptoms suggested the diagnosis of beriberi. On January 18, 1906, at 8 a. m., the patient exhibited a subnormal temperature of 35.1°, the temperature at noon had risen to 36.3°; pulse 86, respiration 38. At 1.30 p. m. the patient died in syncope.

AUTOPSY twenty-two hours after death: Body of medium-sized, normally developed native, about 30 to 40 years old, poorly nourished. *Rigor mortis:* moderate. Post-mortem lividity well marked on the dependent parts of the body. The surface in general is moderately cyanotic. On section of the body, the superficial veins discharge a considerable amount of dark, fluid blood. The muscles are pale-pink, not very moist. The lymphatics are normal. The pleuræ of the lungs are smooth. The *lungs* are inflated and of a very pale-pink color except in the dependent part where they are light-purple. They are highly œdematous and on section a large amount of watery, foamy fluid escapes. The *heart* is markedly enlarged. It weighs 370 grams; the hypertrophy is particularly noticeable in the right ventricle which is also considerably dilated. Its wall has a diameter of about 7 to 8 millimeters. The chambers contain a considerable amount of dark, fluid blood, and in addition chicken-fat clots. The myocardium is of fair consistency and of a pale, gray-pink color. There are no evidences of marked fatty degeneration. The pericardium and endocardium are smooth; no ecchymoses or petechiae being present. The *intestinal serosa* is rather pale, but translucent; appendix, normal. Mesenteric and post-peritoneal glands somewhat

enlarged. The *spleen* is slightly enlarged, moderately indurated, dark, steel-gray externally and on section, dark brown-red. The pulp is quite firm, the trabeculæ widened and the follicles not very distinct. The *liver* is somewhat increased in size, swollen and of increased consistency. Its capsule is smooth, transparent and translucent. Externally, the organ is of bluish-purple color, with numerous yellow streaks and dots visible through the capsule. The cut surface presents the typical picture of a nutmeg liver. Gall bladder and gall ducts normal. *Kidneys:* normal in size. Capsules, smooth, peeling off easily; external color, pinkish-blue. Consistency of these organs increased. On section, the blood vessels are found to be moderately congested. Tubules are decidedly grayish-white, the pyramids are moderately congested. The *gastro-intestinal tract* is normal except that the mucosa of the small, as well as that of the large intestine, is much congested, so that the veins stand out very prominently. The congestion is best marked in the first part of the duodenum. On dissecting out the *popliteal nerve* and its branches on the left side, it is found that the sheathes show numerous ecchymoses. Such ecchymotic spots also extend into the substance of the gastrocnemius muscle. The muscles of the calf in general are very flabby, and of a pale, grayish-pink color. The brain is very pale, the ventricles contain a moderate amount of fluid; otherwise, the organ is normal. Weight of the brain, 1,165 grams.

ANATOMICAL DIAGNOSIS.—*Hypertrophy of the heart, particularly of the right ventricle, œdema of the lungs, chronic cyanotic induration of the spleen, congestion and parenchymatous degeneration of the kidneys, chronic passive congestion of the liver, congestion of the internal mucosa, ecchymoses into the sheath of the left popliteal nerve and branches, general anæmia, chronic, dry beriberi.*

MICROSCOPICAL EXAMINATION.—The noteworthy changes found in sections of the various organs are: *Myocardium,* no marked microscopic changes, except a moderate increase in the perinuclear pigment. *Spleen,* considerable increase in the connective tissue of the trabeculæ and of the pulp, some proliferation of pulp and endothelia, crowding of the pulp spaces with erythrocytes; follicles, very indistinct and ill-defined. *Kidneys,* cloudy swelling of epithelia of uriniferous tubules; fibrosis and obliteration of some of the Malpighian tufts; however, no general increase of connective tissue; fairly numerous hyaline casts in the tubules. *Liver,* great congestion of the intralobular capillaries, atrophy and fatty degeneration of the parenchyma cells in the center of the lobule. Some round cell inflammatory infiltration of the interlobular connective tissue. Gastrocnemius (inner head), some of the muscle fibers have lost both transverse and longitudinal striation and are swollen and almost homogeneous; however, others are perfectly normal in appearance. *Popliteal nerve and branches,* the degeneration of the myelin sheath and axis cylinders is well advanced.

SYMPTOMATOLOGY.

Clinical types of the disease.—From a clinical standpoint, beriberi may be divided into three main types, namely—the acute pernicious, the wet or œdematous, and the dry or atrophic beriberi; however, this classification is somewhat arbitrary. A rudimentary variety of the disease, in which the symptoms are so mild that medical aid is generally not sought, also frequently occurs in addition to these three well-defined types. Malaise, weakness of the lower extremities, and increased heart beat on slight exertion are usually noticed in these cases. These symptoms may speedily and spontaneously disappear, or they may increase in intensity and then lead to one of the well-defined severer types of the disease.

In the acute, pernicious form, the onset of the symptoms is generally rapid. The patient becomes ill, apparently without premonitory symptoms. A feeling of oppression develops in the chest, dyspnœa, forced respiration, evidences of great venous congestion, frequent vomiting, and the signs of rapid heart failure appear and death finally supervenes. The different types of beriberi have been described by observers from all localities where the disease is prevalent, but they vary in their predominance.

A. Plehn[38] recently observed a number of cases of beriberi in German West Africa (Kamerun); they were all of the acute, pernicious type, ending fatally within from twelve to forty-eight hours. However, he states that Lichtenberg previously had seen subacute and chronic cases in the same territory. Plehn's cases, with one exception which was complicated by malaria, never showed any elevation of temperature; they were characterized by dyspnœa, forced, frequent respiration, violent action of the heart, small, easily compressible, rapid pulse, muscular weakness, and violent vomiting. Death occurred from paralysis of the heart after the pulse had become imperceptible.

Both the œdematous and the atrophic types generally develop in the same manner. Preceding the actual outbreak of the disease there is a period of malaise, during which a dull pain in the stomach, lack of appetite, and a heaviness in the lower extremities and occasionally in the upper ones are complained of.

Wright believes that the incubation period of beriberi is between ten and fifteen days, although extreme paralysis and the other more marked effects of the virus may not manifest themselves until some days after the first demonstrable symptoms of nerve lesions have occurred. One of the earliest symptoms usually referred to by the patient, is palpitation of the heart on slight exertion; next, pain in the legs is frequently noticed, particularly in the calves, which soon become tender on pressure. Later, the gait becomes unsteady; the patient walks as if it were difficult for him to lift his feet from the ground, as indeed it is, the effect being such that this gait has not improperly been compared to that of a man walking in soft and very sticky clay, or to that of a man heavily dressed, who has been in the water and whose clothes are weighted by the amount of fluid absorbed. At this stage, in *wet* beriberi, an œdema of the lower extremities is generally noticeable. It is particularly well-marked over the anterior tibial region, over the dorsum of the feet, and around the ankles. In these places the skin pits on pressure. In the *dry* form there may be slight œdema at an early period in the disease, but this is not well marked and is only transitory in character. The lower extremities in this variety, instead of being swollen, become more and more emaciated, the muscles become atrophic, and often indurated

[38] Plehn: Die acuten Infektionskrankheiten bei den Negern der äquatorialen Küsten Westafrikas. *Virchow's Archiv.* (1903), **174**, Supplement (Beriberi, p. 61).

and contracted. Together with the disturbances of locomotion, those of sensation simultaneously develop. Hypæsthesia of the lower extremities is the most common form of disturbance of sensation in beriberi. It generally begins on the anterior, or external, surface of the legs and frequently extends to the dorsum of the feet and toes. In other words, it is found in the regions supplied by the peroneal and saphenous nerves. Accompanying hypæsthesia, there is a subjective paræsthesia. If the skin of the patient is touched with a soft, camel's-hair brush, he has the sensation of paper intervening between the skin and the brush. The intensity and the extent of such sensations not only vary in different individuals but also at different periods of time in the same one. These disturbances have a tendency to extend upward from the feet and legs. In the severer cases, the upper extremities are similary affected. The face is rarely involved, but occasionally disturbances in sensation are found around the mouth. True anæsthesia is rare, as is also hyperæsthesia. The interferences with motility generally begin as a sensation of weakness in the legs, which is first noticed in the calves and later on in the thighs. After these changes have endured for some time, atrophy generally manifests itself, or it may appear even before distinct paralysis becomes obvious. Usually, the anterior, sharp edge of the tibia becomes more prominent, the calf thin and flabby, and the thigh gradually emaciated. When more or less contraction is associated with the atrophy, the foot assumes an equinovarus position. In severe cases, similar changes occur in the upper extremities. Paralysis of the lower extremities is much more common than it is of the upper ones; but in the severest cases both feet and hands, including the toes and fingers, may be paralyzed. In such instances the hands and fingers may occasionally be more affected than the feet. In the gravest types neither the hands nor the fingers can be flexed toward the dorsum, and we have complete wrist drop, as is the case in lead poisoning.

The electrical excitability shows various degrees of change, from a simple diminution to complete degeneration reaction. According to K. Miura,[39] one can predict the result of the electrical reaction from the position and movements of the foot and toes. If the foot can easily be moved on the ankle joint, one finds only a diminution of electrical excitability. If the toes, but not the foot, can be flexed dorsally, we encounter only a partial degeneration reaction, but if neither the foot nor the toes can be moved voluntarily, then it is complete. Paralysis of the diaphragm and of the intercostal muscles occurs only in the severest cases. Other nerves, besides those of the extremities which are so profoundly affected in beriberi, are also more or less frequently involved. Paresis of the muscles of the larynx is by no means rare; in fact, it is a

[39] K. Miura: Notizen zur Symptomatologie der Beriberi. *Centralb. für Neurologie, etc.*, Tokyo, April (1905), 6.

very common occurrence in beriberi to find changes in the voice, such as hoarseness and more or less complete aphonia. Paresis of the facial nerves and of the *nervus abducens* has occasionally been observed, as have also disturbances of the optic nerves, manifesting themselves by central scotoma, and in rare cases by amblyopia. Among the late symptoms of beriberi, which in the advanced disease frequently become quite prominent, are contractions of the muscles, particularly of the gastrocnemius.

If an early examination, both in the hypertrophic and in the atrophic dry types, be made, the following symptomatology may be elicited; the pulse is generally rapid, somewhat irregular, rather weak, and easily compressible. Upon exertion, which may even be so slight as the act of sitting up in bed for examination, the pulse rate increases 20 to 30 beats a minute. At times, quite early in the course of the disease and frequently later, after if has existed for several days, the apex of the heart is found to be displaced upward and outward and the area of visible heart beat to be enlarged. Percussion shows an extension of the area of heart dullness toward the right and frequently even to the right of the sternum. Where there is hypertrophy of the left ventricle the area of dullness is also increased to the left. Auscultation at the apex of the heart frequently reveals some changes in the systolic sound, but the most common alteration observed in beriberi generally is a marked accentuation of the second pulmonic sound. At times a definite, systolic bruit may be heard at the apex; frequently a reduplication of the second sound both at the apex and at the pulmonary valves exists. A considerable number of cases of beriberi also reveal a musical sound which may be heard over the crural arteries as was first prominently pointed out by M. Miura.[40] This observer in some cases reported the sound to be audible even at a distance of several feet from the vessel. In the early stages of beriberi, sometimes up to the sixth or seventh day of the disease, the patellar reflex is increased; then a diminution develops, and finally it becomes entirely absent. Even in cases which terminate favorably, the absence of the patellar reflex may last for a long time and may still be noticeable after the disturbances of locomotion have disappeared. When the knee jerk begins to reappear, it then generally once more becomes temporarily accentuated, finally returning to the normal.

Durham makes the following statements with reference to the patellar reflex in beriberi:

> Too little notice is, I think, taken in most books of the preliminary exaggeration of the knee jerk, which so commonly precedes the loss thereof. Whether the knee jerk is ever lost without a previous stage of increase I am not able

[40] M. Miura: Der diastalische Arterienton. *Zeitschr. d. Mediz. Ges. zu Tokyo*, Jan. (1891), and *Mittheil. d. mediz. Fakultät, Univ. zu Tokyo* (1898), No. 2, 4, 71.

to say, but observations of a number of patients showed that, given the increase, it may remain and never disappear before the patient's apparent recovery, or it may slowly decrease to absolute loss, or it may disappear rapidly in a few days, giving way to complete absence. Recovery of the knee jerk after loss seems to be a very slow process, but that it is eventually regained there can be no doubt, if the history of having had the disease in several prisoners and others is to be believed. Increased response to a blow of the muscles seems to obtain generally after the diminution of knee jerk has occurred.

It has already been mentioned that the muscles of the calves of the leg are frequently painful and very tender to pressure. The skin, particularly of the lower extremities, shows disturbances of sensation. There is general hypæsthesia or paræsthesia and less frequently complete anæsthesia. In mild cases the urine is somewhat decreased in amount, and in severe ones considerably so. The diminution is sometimes very great and the daily amount passed may fall below 100 cubic centimeters. The specific gravity in such cases is increased, but not proportionately to the great diminution in amount. Albumen is generally not present. However, when it is observed, only traces occur. Sometimes, though rarely, a complicating nephritis develops in the later stages of beriberi and then albumen is constantly found in the urine. Indican is very frequently observed in the urine in the acute and œdematous varieties of the disease.

According to most authors, the *temperature* in uncomplicated cases of beriberi is either normal or very slightly elevated. Whenever we have met with a fatal case of this disease, in which there was, *inter vitam*, a marked rise in temperature, on post-mortem examination we have found some complication, generally either amœbic dysentery or malaria. In cases of the œdematous or of the atrophic form, which progress unfavorably, the dyspnœa and the difficulty in respiration increase and the resulting, grave circulatory disturbances find their expression in a superficial venous congestion, with visible, throbbing veins. While consciousness is preserved, the dyspnœa and the suffering, progress, and the face of the patient sometimes presents a picture of grave anxiety, such as may be seen in true angina pectoris (arteriosclerosis of the coronary arteries), and death frequently occurs quickly in consequence of heart failure.

Stanley [41] has drawn attention to the frequency of *sudden heart failure* in diphtheria and in beriberi. His analysis of 341 cases of the latter disease shows 72 fatal ones, of which 31 died of rapid heart failure. The pulse tension was lowered in 254 cases, and dilatation of the heart existed in 98. The second sound was reduplicated in 245 and the first

[41] Arthur Stanley: On Sudden Heart Failure in Toxæmic Conditions with a Special Reference to Diphtheria and Beriberi. *Brit. Med. Journal*, (1903), 2 1636.

in 35. There were cardiac murmurs in 84. In reporting his observations Stanley gives the following graphic description of heart failure and of the heart symptoms in beriberi:

In both diphtheria and beriberi sudden heart failure is the most terrible complication, and one in which, as a rule, no treatment is available in preventing death. * * * In both these diseases the occurrence of vomiting is almost the invariable herald of a rapid, fatal termination by heart failure. Practically speaking, the main signs met with in heart failure occurring in any of these conditions are vomiting, restlessness, lilac-tinted pallor, dyspnœa, increasing weakness of the pulse, and coldness of the extremities. * * * The syncopal attack is marked rather by duration than by intensity; loss of consciousness is rare. * * * The usual time of death from heart failure appears to be about the end of the first week in diphtheria and toward the end of the first month in beriberi. * * * The heart signs of myocardial degeneration are lowered pulse tension, feeble, short pulse wave, feeble heart impulse, short first sound and relatively accentuated pulmonary second sound. The second sound is almost always reduplicated. Reduplication of the first is not unusual and is the cause of the cantering rhythm so frequently met with just before death. Some dilatation of the heart is frequent but not invariable. The cardiac impulse is usually feeble and, when there is dilatation, diffuse. Not rarely the heart's action is bounding and apparently forcible, but the actual circulatory output, as measured by the pulse, is remarkably feeble by comparison, there being a marked difference between the violent overaction of the heart and the small, feeble pulse. Some change in the heart rhythm is invariable; changes in the length of the pauses of the heart cycle being frequent and of great importance in prognosis. Most common is a shortening of the long pause, giving rise to spacing of the heart sounds. The relative shortening of the long pause may be of all degrees up to tic-tac rhythm, where the short equals the long pause, so that the heart sounds are equidistant. The change in the relative length of the two heart pauses is almost always accompanied by a change in the character of the sounds, the first sound becoming like the second in quality, losing its deep, so-called muscular sound, and making more audible the valvular sound, which resembles the ordinary valvular second sound. In this way the two sounds and the two intervals tend to become alike. This tic-tac rhythm caused by the shortening of the long pause—the recuperative intervals—indicates diminished cardiac recuperative power, and prognosticates danger ahead—danger of heart failure. But of worse prognosis is that condition where, in addition to the long pause being shortened, the short pause is likewise shortened, so that the second sound follows very closely on the first. This condition is almost always a fatal sign, and occurs with or may be followed by heart failure. A condition characterized by what may be termed delayed beats or "tumbling rhythm" is a common feature of irregularity of the heart's action, both in diphtheria and beriberi. After a series of regular heart beats, a pause occurs, followed by a sudden scramble of two or more heart beats in order, as it were, to make up for lost time. This gives rise to an intermittent pulse, because all the beats do not reach the pulse.

When the disease ends in recovery, the disturbances of circulation decrease in intensity. In the wet form a profuse secretion of urine occurs and the œdema gradually disappears. In both types which progress favorably, the disturbances of sensation and the paralysis gradually disappear and the patient regains the use of his limbs.

INFANTILE BERIBERI.

Hirota[42] first called attention to beriberi occurring among infants suckled by mothers suffering from *kakke*. He gives a summary of 52 cases which he observed and enumerates the following as the most important symptoms of the condition:

The heart's action is accelerated; the second pulmonic sound accentuated; heart's area of dullness generally increased toward the right side; sound at the apex sometimes dull; pulse rapid, soft, having the character of *pulsus celer;* diastolic arterial sound sometimes heard over the crural artery, dyspnœa and aphonia almost without exception present; vomiting, cyanosis, and œdema occur very frequently; urine generally diminished; indican test sometimes positive, no albumen; general condition characterized by depression, constant crying and groaning; sensorium, clear; no fever. The sensory and motor disturbances of the patients could not be tested on account of their age.

Hirota first medicinally treated a number of cases of this type of beriberi in children, who had been suckled by mothers sick with *kakke,* but without success. However, he soon found that such patients rapidly improved when taken away from their mothers and either given to a healthy wet nurse or fed on artificial food. He therefore recommended this procedure as the only rational therapy. However, it was successful only when the disease had not progressed too far.

The author has made inquiries among a number of practitioners in Manila to ascertain whether beriberi in infants occurs in the Philippine Islands under the same circumstances under which Hirota has observed it in Japan. He has been repeatedly assured, for instance by Dr. Albert, that such cases are not very infrequent. However, the suggested proper therapy—i. e., of taking the child away from a mother (who frequently only shows mild symptoms of beriberi)—is very difficult to carry out in practice, since the people do not understand the necessity for such a measure.

COMPLICATIONS AND SEQUELÆ.

The most common complications of beriberi are tuberculosis and dysentery, and in some localities, malaria. When these conditions coexist the prognosis is usually very grave. Whereas most cases of beriberi end in rapid recovery, some assume a protracted course and in the latter, general weakness with or without anæmia, difficulty in the use of the lower extremities, contraction and induration of the muscles of the calf, and also disturbances of motility in the upper extremities, diminution and disturbance in the quality of the sensation, palpitation of the heart, and rapid pulse may remain present for a long time. As a rule, these symptoms all disappear under proper treatment and diet. It has been

[42] Hirota: Ueber die durch die Milch der Kakke (Beriberi) leidended Frauen Verursachte Krankheit der Säuglinge. *Centralbl. f. Innere Medizin* (1898), **19**, 385; also *Zeitschr. d. Mediz. Ges. zu Tokyo* (1891), **5**.

noticed in Europeans or Americans who have suffered from severe attacks of beriberi and who have returned to their native country during convalescence, that the disease frequently assumes a protracted course, from which recovery is very slow.

DIAGNOSIS AND DIFFERENTIAL DIAGNOSIS.

In many cases of beriberi occurring among the uneducated and ignorant Asiatics, the diagnosis must be made exclusively from the objective symptoms, as an intelligible history is unobtainable. The most important points to be emphasized are the following: The condition of the pulse while the patient is at rest and before he has been at all disturbed; and the same after the patient has been subjected to some physical exertion. If the patient is not too ill, he should be compelled to leave his bed and to walk up and down the room a few times. While so doing, the gait should be noted, in order to ascertain whether it presents the characteristic appearance. The pulse should then once more be counted because it is usually very excitable in beriberi, and its rapidity increases very markedly even on very slight exertion. The percussion and auscultation of the heart are also of special value in the diagnosis of this disease. Particular importance attaches to the enlargement of the right ventricle, to the accentuation of the second pulmonic sound, and to a reduplication of the second mitral one. The presence of hydropericardium, hydrothorax, and abdominal ascites is of considerable value in the diagnosis; the increase of the patellar reflex in the early stages of the disease and the loss of it in the more advanced ones is also important. The frequency of pain in the muscles of the calf and of œdema in the legs and feet has already been referred to in the consideration of the symptomatology. The great decrease or even the suppression of the urine in the early stages of the œdematous form of the affection is also a very important factor in the diagnosis; the disturbances of sensation and of locomotion and the paralysis and contractions have been sufficiently emphasized under the symptomatology. Scheube thinks that the diagnosis of beriberi in a majority of the cases offers no particular difficulty, and that the most important symptoms to be looked for are hypæsthesia in circumscribed places (particularly of the legs and feet), œdema of the legs and of the dorsum of the feet; pain on pressure in the muscles of the calf; absence or increase of the patellar reflexes, palpitation of heart, accelerated, easily excitable pulse, and increase of the number of pulse beats after slight exertion.

Baelz and Miura [43] particularly mention the following among the diseases and their symptoms which might be confounded with beriberi:

Spinal myelitis: Increased reflexes; ankle clonus; paralysis of the extremities without muscular atrophy; paralysis of the bladder and rectum; complete

[43] Baelz and Miura: Beriberi oder Kakke. Mense, *Handb. d. Tropenkrankheiten*, Leipzig (1905), 2, 140.

anæsthesia, without pain in the muscles of the calf; no electric degeneration reaction; no symptoms on the part of the heart and kidneys. In *Landry's paralysis* there is fever at the onset, and pain in the head, with much perspiration at the back and extremities. A study of the sensation and circulation reveals nothing abnormal. *Tabes* usually should not be confounded with beriberi or vice versa. In anæsthetic leprosy a thickening of the peripheral nerves and *true anæsthesia* is found and *not hypæsthesia* which is generally encountered in beriberi. In addition, in leprosy spots or nodules or diffuse thickenings of the skin are usually encountered. Obviously, a careful search will reveal the presence of the leprosy bacillus.

Certain cases of *peripheral nephritis,* depending upon chronic alcohol or arsenic intoxication, may at times be exceedingly difficult to differentiate from beriberi. Alcoholic neuritis should first be definitely excluded before a diagnosis of beriberi is made in Europeans and Americans living in tropical countries, where beriberi is prevalent, and who present symptoms suggesting the possibility of an attack of this disease. In Japan and the Philippine Islands, where beriberi is so frequent and so well known, patients often consult the physician with the simple statement that they are suffering with this disease. But, of course, such a statement can not be accepted without verifying its correctness by a proper examination.

PROGNOSIS.

The prognosis of beriberi varies greatly in different epidemics and in different localities. The disease is generally most fatal, like other infections, when it first invades an entirely new territory in which it has not before been prevalent, or at least not been present for several generations. Scheube emphasizes the great uncertainty of the prognosis in beriberi because, even in apparently very mild cases, a profound cardiac disturbance may suddenly supervene. If this condition appears, then the prognosis always becomes grave. On the other hand paralyses *per se* are not indicative of a fatal issue. The mortality in beriberi also varies very much in different epidemics, localities, and races. Among the Chinese prisoners at Shanghai, according to Stanley, the mortality is 20 per cent, but it has been 50 per cent among the Chinese patients of the Hongkong Government hospitals during the last ten years.[44] The death rate in cases developing in Bilibid Prison at Manila is likewise quite high. However, in these instances the conditions are somewhat exceptional and particularly unfavorable. With better surroundings the mortality from beriberi is usually low. Among the troops in Dutch India the death rate in this disease is given as between 2 and 6 per cent; with the English East Indian troops the figures are somewhat higher. According to Scheube the average mortality in Japan is 3.5 per cent. During the first year (1904) of the late Russo-Japanese war, there were

[44] According to a personal communication from Dr. M. V. Koch, physician in charge of the Government Civil Hospital for Infectious Diseases, Hongkong.

sent from the front to the military reserve hospitals of Hiroshima, Tokyo, etc., 50,340 Japanese soldiers sick with beriberi. Of these 1,024, or less than 2 per cent, died. During the same period of time, among the troops in Japan there developed 3,337 cases, of which only 44 died. So on the whole, taking a very large material as a basis, the prognosis *quoad vitam* is quite favorable in beriberi. However, nothing definite can be stated in an individual case of beriberi, because a fatal termination in consequence of heart failure may occur at almost any time during the course of the disease. Unfavorable symptoms are: marked dilatation of heart, great weakness and irregularity of the pulse and other grave disturbances of circulation, circumscribed œdemas on the trunk of the body, œdema of the lungs, and particularly, persistent vomiting. The last symptom is almost invariably the precursor of a rapid fatal termination, in consequence of heart failure. The mortality in the acute, pernicious form is always very high; in the subacute or chronic, œdematous type it is lower than in the former, but higher than in the dry, atrophic variety. A favorable prognostic omen is the appearance of a copious renal secretion after a partial or complete suppression of urine. Acute, pernicious cases, when fatal, always terminate by heart failure or asphyxia; in chronic cases death results from paralysis of the respiratory muscles, but occasionally from aspiration pneumonia or from general debility. The latter event is particularly liable to take place when tuberculosis or amœbic dysentery is present as a complication. The average duration of the cases of acute, pernicious beriberi is very short, while that of those of moderate intensity and of a moderately chronic character is perhaps between three and six weeks. Besides the above there are a large number of protracted cases, which extend over a period of months or even more than a year. These are characterized by muscular atrophies and joint fixations. However, generally even these cases, if properly treated and if placed under proper hygienic conditions and given proper nutrition, finally completely recover.

It has frequently been noticed in Japan, the Malay Peninsula, and the Philippine Islands that if a patient who has had one attack of this disease, and has completely recovered, is exposed to the same conditions which brought on the first one, he suffers a second or even a third attack. In this respect beriberi may perhaps be likened to pneumonia and some of the other infectious diseases, which, in certain individuals after the first attack, leave a predisposition to subsequent ones.

PROPHYLAXIS.

Our ideas on prophylaxis, in relation to beriberi, are still in a decidedly unsatisfactory state. The observance of the ordinary rules of hygiene and sanitation has frequently shown a favorable influence in restricting the spread of the disease. However, in other instances, beriberi will prevail in certain localities and under certain conditions, in spite of all

hygienic and sanitary measures. The late Russo-Japanese war furnishes a confirmatory example of this statement. The hygienic measures adopted in the Japanese army proved sufficient to limit to a minimum such diseases as typhoid, typhus, dysenteries, scorbutus, etc., but they were of no avail against beriberi. Beyond all doubt there is one factor which favors the occurrence and spread of beriberi in those countries and among those races where it is at all prevalent, and that is the crowding together of large numbers of persons into limited spaces, as in prisons, barracks, schools, factories, mines, and ships. If beriberi appears under such environment, the situations should, if possible, be abandoned as dwellings, or at least the number of inmates should be decreased and a thorough disinfection, airing, and drying should be undertaken. The statements in regard to the effects of a change from a rice diet to some other, as a prophylactic against beriberi, are up to the present time so hopelessly contradictory that reliable conclusions can not be drawn from them. Women sick with beriberi should not nurse children. Scheube recommends as prophylactic measures, draining of the soil, a rational sewer system, proper hygiene as to the supply of drinking water, ventilation of houses, removal of beriberi patients, examination of ships before departure and detention of persons afflicted with beriberi or suspected of having the disease.

TREATMENT.

There is no specific treatment for beriberi. A patient suffering from this disease should be confined to bed. Even in mild cases in the early stages of the disease, rest should be insisted upon, since it is important to reduce the heart's action as much as possible, in order to guard against future and often unexpectedly grave cardiac complications. It has generally been found very advantageous to administer the saline laxatives in large doses during the first stages of beriberi. A favorite Japanese prescription, used very extensively, is the following:

℞

Magnesii sulfurici	30 to 50 grams.
Acidi muriatici diluti	1.5 to 2 c. c.
Tincturæ amaræ	4 c. c.
Aq. dest. q. s. ad.	200 c. c.

M. D. S. 30 c. c. three times per day.

This treatment should be continued during five to seven days, followed by an intermission of a few days, after which it should be repeated. Other laxatives and purgatives recommended are cream of tartar, infusion of senna, Carlsbad salt, castor oil, and aloes and jalap pills. Where there is marked œdema, Baelz and K. Miura recommend potassium acetate, potassium nitrate, or diuretin. Scheube has strongly advocated the use of digitalis in beriberi, but most other observers consider it of very doubtful value, and it has repeatedly been stated that in many cases it has a decidedly injurious effect in that it helps to produce

vomiting, great anorexia, and nausea. In severe, acute cases with great weakness of the heart, Baelz frequently observed good effects from large doses of cocaine given internally in amounts of from 0.05 to 0.15 or 0.20 grams per day. In acute or subacute cases, with signs of dilatation of the right side of the heart, while the pulse is still good, encouraging results have been obtained by withdrawing several hundred cubic centimeters of blood from the median cephalic vein. However, when the pulse has become weak, this procedure is dangerous, because of the possibility of sudden heart failure. In the presence of dilatation, venous congestion and a pulse which is already weakened, the withdrawal of blood by the aid of cups or leeches, applied over the precordial region, is often followed by a speedy amelioration of the symptoms of circulatory disturbance and of the difficulty of respiration. The author has seen a considerable number of Japanese soldiers sick with beriberi who were greatly benefited by this method of bloodletting. However, the improvement is frequently only temperary and a repetition of the procedure may or may not bring about good results, or the unfavorable symptoms may increase in severity in spite of a temporary amelioration.

Where there is a very marked hyperæsthesia (which, however, is rare in beriberi), bromide of potassium or morphia internally or chloroform externally are recommended. Vomiting and dyspnœa are frequently greatly ameliorated by the hypodermic administration of small doses of morphia.

It is very important that the muscular atrophies and contractions, so common in beriberi, should receive early and proper treatment. However, it is not advisable to begin the latter as long as there is marked œdema of the affected extremities. When the œdema has subsided, massage and passive movement are to be systematically practiced several times a day. As soon as the patient is able to do so, and when there is no longer any immediate danger of cardiac failure, moderate, active exercise should cautiously be begun. Should such exercise lead to a very marked increase in the pulse rate, it should be postponed. The atrophic muscles are to receive electrical treatment. When they still react to the Faradic current, the latter is to be used. Where there is complete degeneration reaction, the galvanic one should be employed, with the cathode situated peripherally over the nerve and the anode centrally applied. In the use of the Faradic current, Scheube recommends large sponge or roller electrodes, to be employed in a massaging manner. When there is paralysis of the phrenic nerve, M. Miura advises faradization, one sponge electrode being placed over the epigastric region and the other above and inside of the sterno-clavicular articulation, or the two electrodes may both be placed on the sides of the neck.

The diet in beriberi should be light and nutritious and should include a considerable quantity of milk. Both in Japan and in Java beriberi patients frequently receive the *adzucki-bean* (*Phaseolus mungo* var.

radiatus Bak.) as a part of their daily nourishment, and it is believed that this has both a favorable prophylactic and a curative tendency. In the Philippines, similar virtues are claimed for the *mongo* or *mungo-bean* (*Phaseolus mungo* L.). Rice should, in private practice at least, be entirely withdrawn from the daily diet of the patient. Alcohol in any form is considered inadmissible in the treatment of beriberi and it should be entirely withheld. A person sick with a severe type of beriberi, accompanied by grave circulatory disturbances, should not under ordinary conditions be removed to a distance. Even during the early stages of recovery, a long railroad journey may bring on a relapse with severe and dangerous heart symptoms. Cases which are mild from the onset and serious ones after complete recovery, may with advantage be removed from a beriberi-infected neighborhood to a high and dry locality free from this disease, and a change of climate and return to a more bracing atmosphere should be recommended to Europeans and Americans who have suffered an attack.

CONCLUSION.

(1) Beriberi, kakke, or *neuritis multiplex endemica* is an acute, subacute, or chronic disease, generally only prevalent in certain well-defined territories. It is clinically characterized by disturbances of circulation, of motion, and of sensation.

(2) Its most pronounced anatomical lesions are, first, hypertrophy and degeneration of the myocardium and degeneration of the peripheral nerves and skeletal muscles, and second, localized or more or less general œdema, parenchymatous degeneration of the kidneys, liver, and interstitial hepatitis.

(3) Beriberi is neither primarily a nutritional disturbance nor a simple intoxication like lead, alcohol, arsenic, or similar intoxications accompanied with multiple peripheral neuritis, but is an infectious disease.

(4) Our animal experiments and blood examinations appear to indicate very strongly that none of the claims brought forward for the discovery of a specific micro-organism for the disease can be looked upon as substantiated.

(5) While, in the absence of any positive evidence or proof, it is perhaps dangerous to venture on an hypothesis, I would like to express the belief that beriberi is due to an organism which gains entrance into the human body, either directly or through food, and there produces a toxin which in character and effect is similar to the diphtheria or tetanus toxin and which by an accumulative action gives rise to the well-characterized anatomical and histological lesions of beriberi.

ILLUSTRATIONS.[45]

PLATE I. Japanese soldier in the Hiroshima Kakke Hospital. Dry, atrophic beriberi with advanced muscular atrophies, contractions, and *pes equinovarus*.

II. Japanese soldier in the Hiroshima Kakke Hospital. Dry, atrophic beriberi. Paresis of the extensor muscles of the arms.

III. Native Filipino, prisoner in Bilibid Prison, Hospital B. Chronic, wet beriberi. Œdema of the legs and of the dorsum of the feet.

IV. Three native Filipinos, prisoners in Bilibid Prison and patients in the Main Prison Hospital. Chronic, wet beriberi. Œdema of the legs and of the dorsum of the feet.

V. Native Filipino, Constabulary private. Acute, wet beriberi. Great œdema of the legs and feet.

VI. Fig. 1. Acute, pernicious beriberi (Necropsy No. 1547). Longitudinal section of the popliteal nerve; Weigert-Pal stain. Showing degeneration of the myelin sheath. Low magnification.

Fig. 2. Acute, pernicious beriberi (Necropsy No. 1547). Longitudinal section of popliteal nerve; Weigert-Pal stain. Showing rosary formation and honeycombing of myelin sheath. Medium magnification.

VII. Fig. 1. Acute, pernicious beriberi (Necropsy No. 1547). Longitudinal section of popliteal nerve; Weigert-Pal stain. Showing various types of degeneration of the myelin sheath. Medium magnification.

Fig. 2. Acute, pernicious beriberi (Necropsy No. 1547). Transverse section of popliteal nerve; Weigert-Pal stain. Showing varying degrees of degeneration of the myelin sheath. Medium magnification.

VIII. Fig. 1. Subacute beriberi (Necropsy No. 1636). Longitudinal section of popliteal nerve; Weigert-Pal stain. Showing profound degeneration of the myelin sheath. Medium magnification.

Fig. 2. Subacute, wet beriberi (Necropsy No. 913). Longitudinal section of popliteal nerve. Hæmatoxylin-eosin stain. Showing proliferation of neurolemma nuclei. Medium magnification.

IX. Acute, wet beriberi (Necropsy No. 1225). Section of myocardium. Hæmatoxylin-eosin stain. Showing fragmentation and segmentation. Medium magnification.

X. Fig. 1. Subacute, wet beriberi (Necropsy No. 913). Section of the myocardium. Hæmatoxylin-eosin stain. Showing loss of striation vacuolation, and granular degeneration. Medium magnification.

Fig. 2. Acute, pernicious beriberi (Necropsy No. 1595). Section of the liver. Hæmatoxylin-eosin stain. Showing fatty degeneration and necrosis in the central area of the liver lobule. Medium magnification.

[45] The photographs of beriberi patients are from the author's original plates, taken in Hiroshima, Japan, and in Manila, P. I. The microphotographs are by Charles Martin, photographer of this Bureau, from sections prepared and stained by F. H. Willyoung, of the Biological Laboratory, Bureau of Science.

XI. Fig. 1. Subacute, wet beriberi (Necropsy No. 913). Section of liver. Hæmatoxylin-eosin stain. Showing fatty degeneration and necrosis in the central area of the liver lobule. Medium magnification.

Fig. 2. Subacute, wet beriberi (Necropsy No. 1536). Section of the liver. Hæmatoxylin-eosin stain. Showing interlobular, periportal inflammatory focus. Medium magnification.

XII. Fig. 1. Acute, pernicious beriberi (Necropsy No. 1547). Section of stomach. Methylene blue-eosin stain. Profound eosinophilia of mucosa. Oil immersion.

Fig. 2. Acute, pernicious beriberi (Necropsy No. 1547). Section of duodenum. Methylene blue-eosin stain. Profound eosinophilia of mucosa. Oil immersion.

PLATE I.

PLATE III.

PLATE IV.

PLATE V.

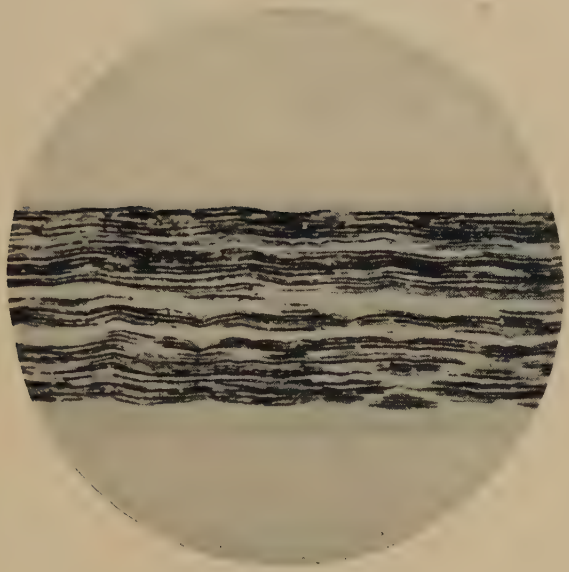


FIG. 1.

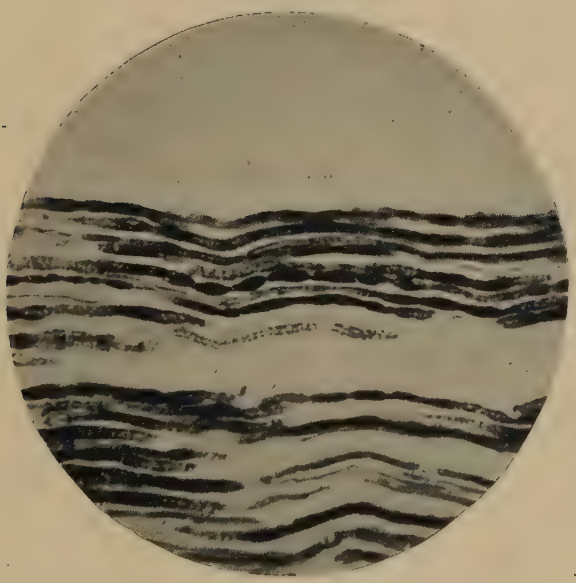


FIG. 2.

PLATE VI.

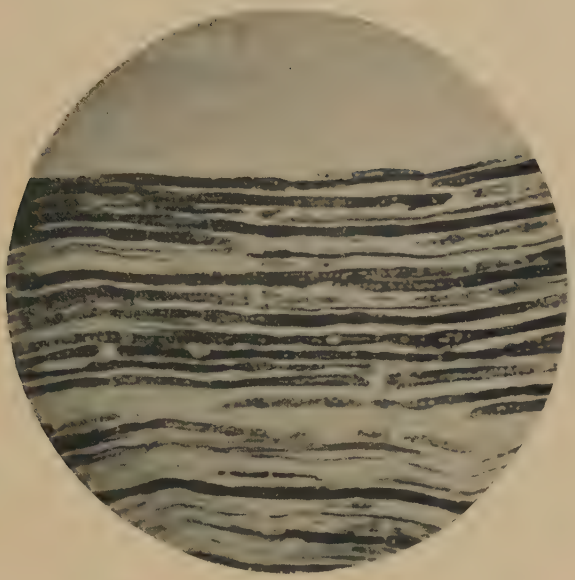


FIG. 1.

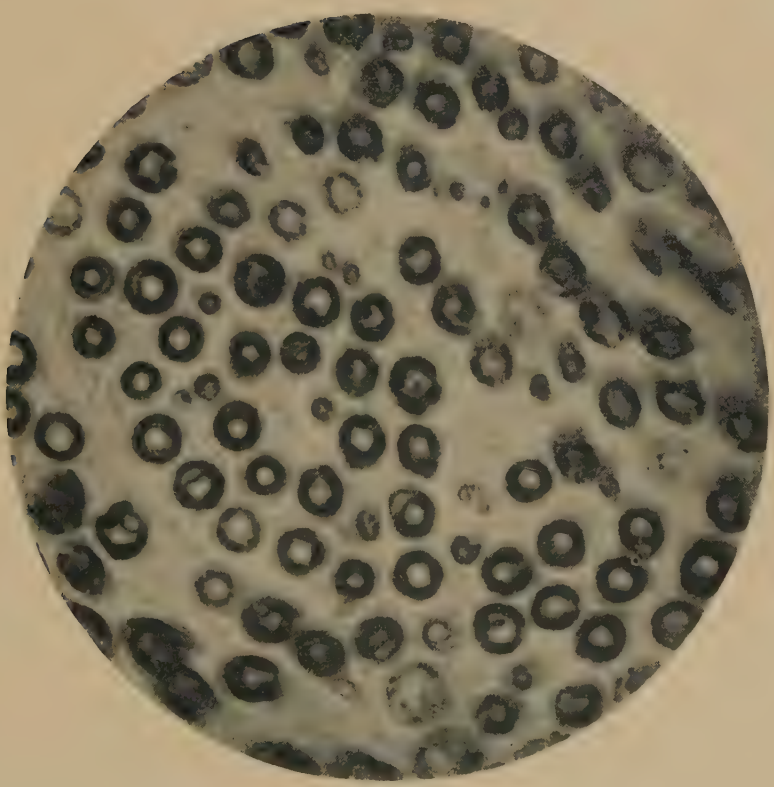


FIG. 2.

PLATE VII.

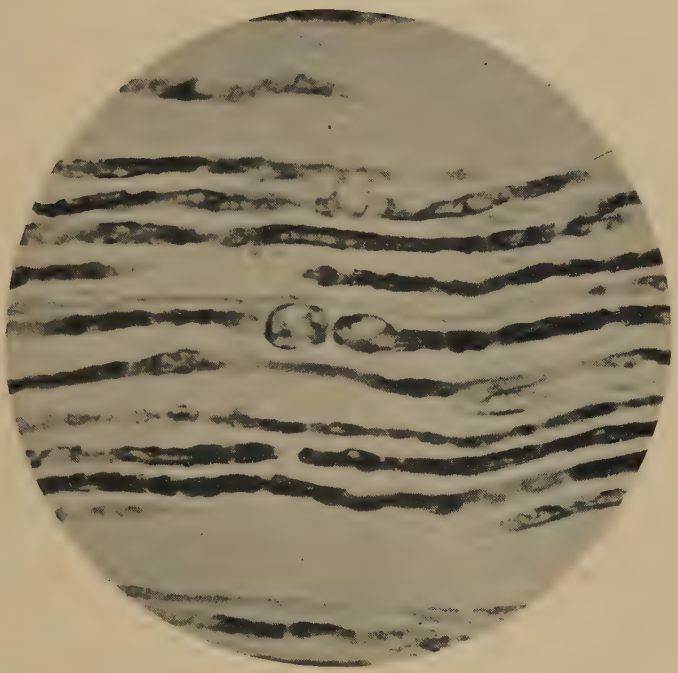


FIG. 1.

FIG. 2.

PLATE VIII.

PLATE IX.

FIG. 1.

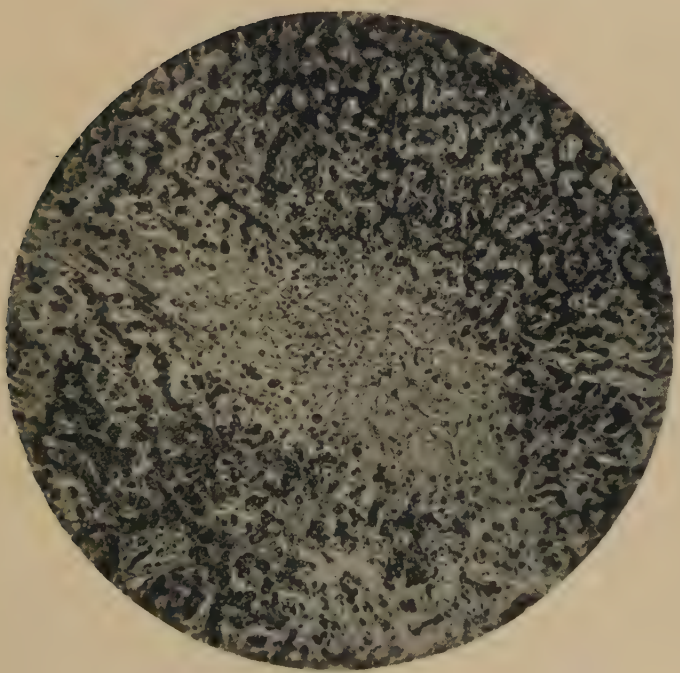


FIG. 2.

PLATE X.

FIG. 1.

FIG. 2.

PLATE XI.

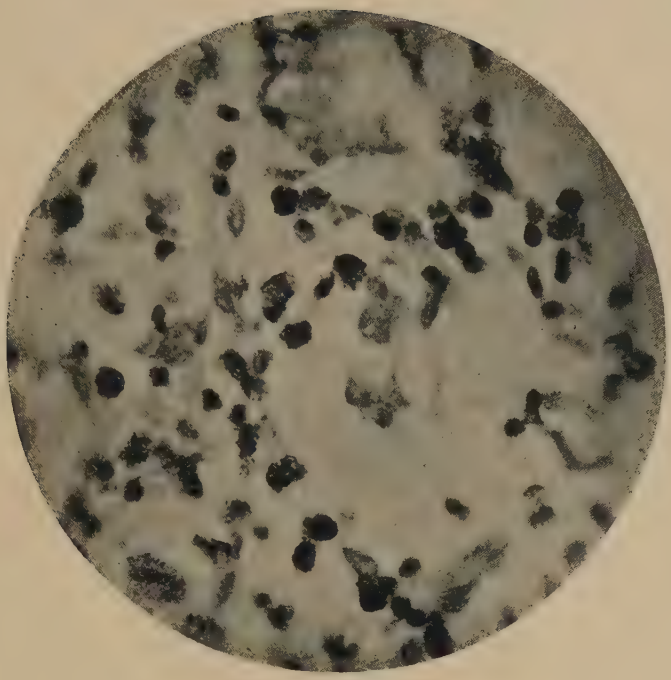


FIG. 1.

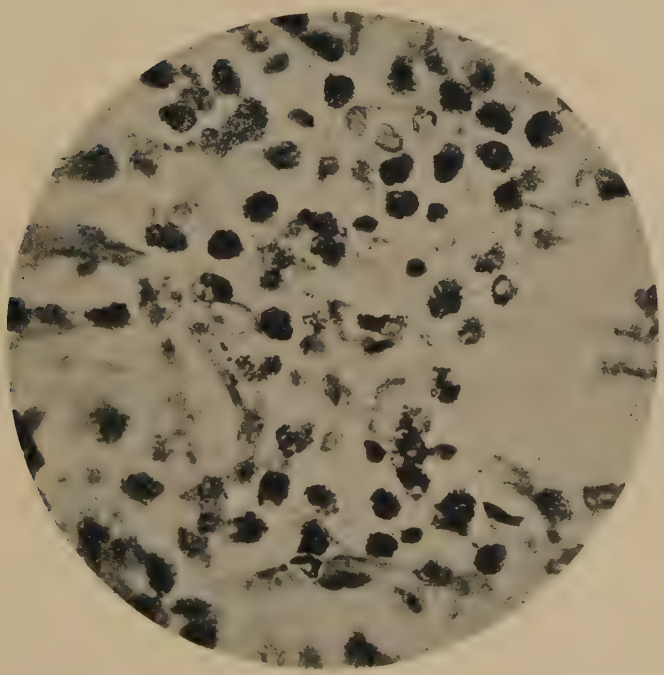


FIG. 2.

PLATE XII.

NOTES ON FOUR BIRDS FROM LUZON AND ON A SPECIES OF DOUBTFUL OCCURRENCE IN THE PHILIPPINES.

By RICHARD C. MCGREGOR.

(*From the zoölogical section of the Biological Laboratory of the Bureau of Science, Manila, P. I.*)

Strix candida Tick.

Two adult females and a full grown young barn owl were purchased in Manila February 15, 1906. They were said to have been taken at Biñang, La Laguna Province, Luzon.

The young bird, doubtless captured on the nest, is heavily covered with light, ochreous down; face brown; feathers of ruff white with blackish brown tips; rectrices and remiges partly developed. This specimen is of interest as it establishes the fact that the barn owl breeds in the Philippines. The eggs must have been deposited early in January.

Antigone sharpei Blanf.

Mr. Worcester, in a letter dated April 25, 1906, has sent me the following interesting notes concerning the habits of the above species in northern Luzon:

It may interest you to know that I saw *Antigone sharpei* in large numbers in Cagayan and Isabela during my recent trip through those provinces. I am informed that these birds nest on the ground in May, contenting themselves with scraping together and flattening down a little grass on which to deposit their eggs. About August they lose their long wing feathers and when in this condition can rise but a few feet from the ground. The people of Isabela then pursue them on horseback and take them with lassoes, although according to the statements of the hunters the birds, aided by their wings, run about as fast as deer.

Herodias timoriensis Less.

While examining some mounted birds at the shop of a Filipino taxidermist I saw a white heron which belonged to the above species. It was still fresh, having been killed the previous week. I noted the following data:

Killed on the Laguna de Bay, Luzon, March 16, 1906. Sexed by the taxidermist as a male. Entire legs and feet black; bill yellow. Dorsal plumes reaching little beyond base of tail, the bird being in rather poor plumage. Tarsus, 6.25 inches; bill from gape, 5.5; culmen from frontal feathers, 4.5.

This species has not previously been recorded from Luzon, but a specimen was obtained in Mindanao by Mearns and recorded in Proceedings of the Biological Society of Washington (1905) **18**, 89.

Platalea minor Temm. and Schl.?

I am creditably informed of the recent occurrence of a spoon-billed ibis in Luzon, although I have been unable to examine a specimen myself. A Filipino taxidermist tells me that he saw specimens which were obtained in January, 1905, not far from Manila.

The plumage was white; the chin, lores, and a restricted area about the eyes were unfeathered; the legs and feet were dark brown. Some six birds were killed at one shot, but, unfortunately, they were eaten and neither skins nor any other parts were preserved. As this taxidermist is familiar with Philippine birds, I feel sure that his statements are reliable.

The spoon-billed ibis has been reported from Luzon, but we have no certain evidence as to which species occurs, and none of the recent collectors have seen it. We should be very grateful to anyone sending a specimen or even parts of this bird to this Bureau, with particulars relating to the date and place of capture. For the use of those likely to encounter the species, I subjoin a short compiled description of *Platalea minor:*

Plumage entirely white with a small crest; forehead, chin, side of face, and area about eye unfeathered; bill, slate color, transversely barred with black; inside of mouth black; bare skin of face black with a bright-yellow ochre patch before the eye; iris blood-red; legs purplish black. Length from tip of bill to tip of tail, 27 inches; bill, 7.2; last joint of wing, 14.6; tail, 4.2; tarsus (i. e., from base of toes to next joint of leg), 4.75. The spoon-bill is easily distinguished by the shape of its bill, which is spatulate. The spoon-billed, or more properly the shoveler, duck has a similarly shaped bill but in other respects bears no resemblance to the spoon-billed ibis.

Chaetura sp.?

I have received the following note from Mr. Worcester relative to the occurrence in northern Luzon of a giant swift:

On the evening of March 25, just below the Tinguiane settlement of Dipadi on the Ablug River, in the region commonly known as Apayao, I saw a flock of giant swifts of the genus *Chaetura,* numbering some forty individuals. Nearly all of them were flying in pairs, there being apparently only two or three old bachelors in the flock. The individuals of the several pairs did not seem to be pursuing each other but were apparently flying together for the sake of sociability. They were flying very low, occasionally skimming along the surface of the river and dipping into the water as they flew. Several individuals passed within twenty or thirty feet of me. It was most aggravating to be obliged to lose this very exceptional opportunity for collecting giant swifts, but as I had no shotgun with me I had to content myself with observing them as carefully as possible. I looked in vain for the white spot in front of the eye, which is so characteristic a marking of *Chaetura dubia,* recently discovered by you in Mindoro. However, the flight of these birds was so extremely swift that this marking may have been overlooked. All the individuals which were seen showed white markings on the under tail coverts and flanks. There was no light marking on the rump.

NOTES ON BIRDS FROM APO ISLAND.

By Richard C. McGregor.

Mr. Worcester, on November 26, 1905, accompanied by two Filipino collectors from the Bureau of Science, made a landing on Apo, a small coral island 24 miles west from Sablayan, the point nearest thereto on the Mindoro coast.

Specimens of five species of birds were secured; with the exception of *Endynamis mindanensis* these are all migratory species and none of them gives us any clue to the zoölogical relationship of Apo.

Endynamis mindanensis (Linn.).

A male of the Philippine koel.

Turdus obscurus Gmel.

An adult male of this thrush. Mr. Worcester writes to me that "there was a great flock of the thrushes, of which we secured a single good specimen on Apo Island. They were evidently migrating and had stopped in this place to rest."

Acanthopneuste borealis (Blas.).

One specimen of the northern willow warbler.

Horornis canturiens (Swinh.).

A male specimen of this grass warbler.

Anthus maculatus Hodgs.

A male of the spotted pipit.

NOTES ON A COLLECTION OF BIRDS FROM BANTON.

By Richard C. McGregor.

Banton is a small island situated some 16 miles directly north of Tablas. It has an area of 11 square miles. It is of volcanic origin and seems to be surrounded on all sides by deep water. Its surface is quite broken, the highest hills reaching an altitude of about 900 feet. Practically all of its forest land has been more or less completely cleared. There are numerous coconut groves on the island, and there is also an abundance of low scrub with occasional large trees, more or less completely isolated.

As no ornithological collector had ever before visited Banton, Andres Celestino, an assistant collector of natural history specimens in the Bureau of Science, was sent to that island in July, 1905. He collected during the period between July 23 and August 12, obtaining specimens of twenty-one species of birds.

Of these, *Otus romblonis* may or may not be of significance. At present we have too little knowledge of the distribution of this species to draw any conclusions from this occurrence. *Ceyx bournsi,* while unknown from the islands north of Banton, is so widely distributed that its presence there is of little importance. The presence of *Loriculus philippensis, Iole philippensis,* and *Zosterops meyeni* indicates a close relationship between Banton and the Luzon-Marinduque group.

LIST OF BIRDS FROM BANTON.

Streptopelia dussumieri (Temm.).

Two specimens of Dussumier's dove.

Chalcophaps indica (Linn.).

A female specimen of the Indian bronze-winged dove.

Otus romblonis McGregor.

Three small owls, two males and a female, from Banton Island do not differ from the type of the above species. The male has not been described but it is exactly like the female in coloration. Number 11046 in the Bureau of Science collection is hereby designated as the male type.

Measurements of Otus romblonis from Banton Island.

Number.	Sex.	Date.	Wing.	Tail.	Tarsus.
11046	♂	Aug. 3	6.25	3.50	1.12
11047	♂	July 25	6.25	3.13	1.20
11048	♀	July 27	6.35	3.40	1.28

Loriculus philippensis (P. L. S. Müll.).

Four males from Banton July 23–28; two are in immature plumage, the others do not differ from specimens of *L. philippensis* from Luzon.

Ceyx bournsi Steere.

One specimen of Bourns's kingfisher appears to be typical.

Halcyon chloris (Bodd.).

One specimen.

Salangana troglodytes (Gray).

One specimen taken July 29.

Salangana marginata (Salvad.).

A small swift taken July 25 is undoubtedly of this species.

Hierococcyx fugax (Horsf.).

A female from Banton, July 28.

Centropus viridis (Scop.).

Several specimens.

Cyornis philippinensis Sharpe.

One specimen.

Hypothymis occipitalis (Vig.).

One specimen.

Rhipidura nigritorquis Vig.

One specimen.

Lalage niger (Forster).

A nest holding two large young was taken on Banton July 30. (Pl. II.)

This nest is an extremely slight structure with a very shallow cup, reminding one of a dove's nest. The material of which it is constructed consists of small plant stems and tendrils with which are mixed a few bits of bamboo leaves; there is no lining. The nest is 3 inches across the top and is but an inch deep by outside measurement.

The two young which were nearly ready to leave the nest, are slate-brown above, most of the feathers widely tipped with ochreous brown, those of the back with a darker, subterminal band. The wing and tail feathers are black, with wide white, or buffy-white, edges; lower parts white, spotted with black on the chin, throat, breast, sides, and under tail coverts, these spots largest on the forebreast.

Iole philippensis (Gm.).

Eleven fruit-thrushes from Banton, July 23 to August 12, are a trifle lighter in color than Luzon specimens, but the difference is very slight; in measurements they are much nearer *philippensis* than *guimarasensis*, as may be seen by an

examination of the accompanying table. The specimens from Banton are in very poor plumage, so that lengths of wing and tail are of little value but they are here given for the sake of completeness. The interesting fact is that the Banton bird is neither *cinereiceps* nor *mindorensis*, although either of these species might have been expected to occur in Banton, judging from its position.

Average measurements of Iole guimarasensis and Iole philippensis.

No. of skins.	Locality.	Wing.	Tail.	Exposed culmen.	Bill from nostril.	Tarsus.
10	Masbate and Ticao	4.20	3.55	0.92	0.67	0.82
10	Mariveles	3.94	3.55	.81	.61	.78
5	Banton	3.82	3.62	.85	.61	.76

Megalurus ruficeps Tweedd.

Three specimens.

Artamus leucorhynchus (Linn.).

A male and a female.

Zosterops meyeni Bp.

I can not distinguish specimens of the silver-eye of Banton from numerous specimens collected in Calayan, Lubang, Verde, and in Tarlac Province, Luzon. Specimens from Benguet Province, Luzon, seem to be more dusky and may more closely resemble *Zosterops whiteheadi* of Lepanto Province than *Z. meyeni* of Manila and vicinity. However, all of our Benguet specimens are more or less darkened from feeding in burned timber and none are in fine plumage.

Young birds of various sizes collected in Banton, July 24 to August 2, do not differ in color from the adult, except that the yellow throat patch is slightly lighter.

Two eggs taken July 25 are pale blue and unspotted; they measure in inches: 0.62 by 0.49 and 0.68 by 0.49. A nest taken July 29 and containing one egg is composed of fine, yellow, plant fibers without lining; inside depth, 1.5 inches; inside diameter, 2 inches. The egg is pale blue and unspotted; it measures 0.61 by 0.49 inch. (Pl. III.)

Munia jagori Martens.

One specimen.

Oriulus chinensis Linn.

Two females; one in badly worn plumage was taken July 30.

Sarcops calvus (Linn.).

Five specimens of the bald-headed starling from Banton; in a male (No. 10815 ♂) the chin and lores are light seal brown and two feathers on the throat are pure white. Another specimen (No. 10814 ♀) shows the same variation in color of lores and chin. Two others have a few brown feathers on the lores. No other specimens in our large series from other islands show similar variations.

NOTES ON A COLLECTION OF BIRDS FROM THE ISLAND OF TABLAS.

By Richard C. McGregor.

The birds of Tablas have heretofore been known only from the collection made on this island in 1892 by Mr. Worcester, aided by one native collector. Two of the new species discovered by Worcester in Romblon, namely, *Iole cinereiceps* and *Dicaeum intermedium,* were found by him to inhabit Tablas also, while two additional new species, *Rhipidura sauli* and *Chibia menagei,* were discovered, the latter being by far the most remarkable representative of its genus known to inhabit the Philippine Islands.

As Tablas is an island of some size and still has a considerable area of undisturbed forest remaining on the slopes of the high hills and low mountains in its interior, it was hoped that other new species might be discovered there, especially as Worcester was ill during the greater part of his stay on the island and was consequently unable to do any collecting himself.

Two assistant collectors from the Bureau of Science were accordingly sent to Tablas, but although they worked diligently from August 15 to September 30, 1905, they did not discover any new species.

They did secure a fairly good series of specimens belonging to all of the new species discovered by Worcester and increased those known to inhabit Tablas by four, namely, *Osmotreron axillaris, Gallicrex cinerea, Pernis ptilonorynchus,* and *Salangana marginata.*

LIST OF SPECIES COLLECTED.

Osmotreron axillaris (Bp.).

Three specimens.

Phapitreron nigrorum Sharpe.

Eleven specimens.

Leucotreron leclancheri (Bp.).

Six specimens.

Muscadivora ænea (Linn.).

The "balud" of Tablas probably belongs to the variety *calybura* which seems to be fairly distinct from true *ænea* of Borneo.

Streptopelia dussumieri (Temm.).

Two specimens of this common dove were taken in Tablas.

Gallicrex cinerea (Lath.).

Four eggs from Badajos, September 4, 1905. Measurements in inches: 1.53 by 1.11; 1.50 by 1.09; 1.58 by 1.12; 1.56 by 1.10. Surface smooth, with a light gloss; ground color, creamy-white. The few spots are of medium size, irregular in outline and are scattered over the entire surface; in color they are dull lavender and dull reddish-brown.

Lophotriorchis kieneri (Geoffr.)?

A hawk from Badajos seems to be an immature male of the above species. The following notes sufficiently characterize the specimen:

Lores and a wide stripe above eye black, separated from the cere by an extension of the white forehead patch, which also extends backward in a narrowing line above the black eye stripe; long crest feathers blackish, with light tips; rest of upper parts brown, nearly all the feathers with white or at least whitish tips, most pronounced on crown, and secondaries and their coverts; head and neck lightest brown, wings much darker; primaries and coverts, secondaries, and rectrices almost black, the last with conspicuous white tips and banded as in the adult, but more distinctly; quills also barred as in adult; entire lower parts pure white except a patch of light-brown feathers on each flank.[1]

Spilornis panayensis Steere.

A male was obtained on Tablas September 12.

Haliaëtus leucogaster (Gm.)?

A specimen from Tablas is probably the young of this species but it does not agree very well with the descriptions. The identity of this specimen does not in any away affect the known distribution of the species, as the white-bellied eagle undoubtedly occurs in Tablas.

Pernis ptilonorhynchus (Temm.).

A female of the honey buzzard from Tablas, taken September 14, is extremely pale in coloration, the short, scale-like feathers of the lores being much lighter than in any of four other skins at hand. This great difference might lead one to suspect that they represent two species were it not for the known variation in this genus. Newton in his article on the honey buzzard in the Dictionary of Birds, page 427, says:

"The species is still further remarkable for the great difference of coloration exhibited by individuals belonging to it, which have hitherto defied all attempts at reduction to what passes for "law"; but the widest variation is observable in young birds of the year, while the assumption of an ashy-grey head is held to indicate maturity."

Prioniturus discurus (Vieill.).

Five specimens.

Tanygnathus lucionensis (Linn.).

A male from Badajos.

[1] An adult male of *Lophotriorchis kieneri* taken in Sibuyan, June 13, 1904, was accidentally misnamed on the tag and therefore omitted from my paper on birds of Sibuyan in *Publications of the Bureau of Government Laboratories* (1904), 25.

Loriculus bournsi McGregor.

Among 24 specimens of this species from Tablas there are but 4 adult males and even these are not in perfect plumage. They show the characters assigned to this species.[2]

Eurystomus orientalis (Linn.).

A male of the oriental roller from Badajos, Tablas, August 22.

Ceyx bournsi Steere.

A pair of the Bourns's kingfisher.

Halcyon chloris (Bodd.).

Three specimens of the common green kingfisher.

Halcyon winchelli Sharpe.

Three specimens of Winchell's kingfisher.

I think the one described by Sharpe[3] was an immature bird. At any rate the adult male is pure white below, as illustrated by a specimen in the present collection from Tablas, August 31. The other two skins are marked female and are in moult, the lower parts fawn color as described.

Merops americanus P. L. S. Müller.

Three specimens from Badajos, September 12, 1905.

Salangana marginata (Salvad.).

One specimen from Badajos, September 6.

Cacomantis merulinus (Scop.).

One specimen in mixed plumage, September 13.

Eudynamis mindanensis (Linn.).

Two males and a female.

Centropus viridis (Scop.).

Six specimens.

Xantholaema roseum (Dumont).

Nine specimens of the rosy barbet were collected.

Pitta erythrogaster Temm.

One specimen.

Pitta atricapilla Less.

The black-headed ground-thrush appears to have been abundant in Tablas, as the collection contains ten specimens, in fine plumage.

Cyornis philippinensis Sharpe.

Two specimens.

Hypothymis occipitalis Vig.

One specimen.

Rhipidura nigritorquis Vig.

One specimen.

[2] McGregor: *Publications of the Bureau of Government Laboratories* (1904), 23, 16.

[3] *Cat. Bds.*, 17, 255.

Rhipidura sauli Bourns & Worcester. (Pl. V.)

Three specimens of Saul's fantailed flycatcher.

Zeocephus rufus (Gray).

Two pairs of the rufous flycatcher.

Artamides mindorensis Steere.

Four specimens.

Lalage niger (Forster).

One specimen.

Iole cinereiceps Bourns & Worcester.

Twenty-one specimens of this fine species from Badajos, August 15 to September 29.

Pycnonotus goiavier (Scop.).

A male.

Copsychus mindanensis (Gm.).

An adult male from Badajos, September 4; two full-fledged young from the same locality, September 8. The adult male has bill and tail considerably longer than a male from Quisao, Luzon. The young differs from the adult as follows:

Head, neck, and back dull black; chin, throat, and forebreast dull black with a whitish spot on each feather; a few glossy, blue-black feathers of the adult plumage on breast, back, and rump.

A set of three eggs from Badajos, August 15, have the following characteristics:

Pale green, very heavily blotched with dark lavender and olive-brown; spots crowded about the larger end and nearly covering the ground color. Measurements in inches: 0.92 by 0.70; 0.92 by 0.70; 0.94 by 0.70.

Megalurus ruficeps Tweed.

Three specimens.

Acanthopneuste borealis (Blas.).

One specimen from Badajos, September 13.

Artamus leucorhynchus (Linn.).

A female.

Otomela lucionensis (Linn.).

Four specimens of the Luzon shrike from Badajos. This and previous records of *O. lucionensis* made by me are not satisfactory, as many of the specimens are, without doubt, something else. Birds with the upper parts earthy brown and the frontal half of the head grayish white, may be referred with confidence to *O. lucionensis*. However, there are other specimens with no white frontal band and with the upper parts strongly cinnamon-brown or even rufous, these can not be named without comparison with well-determined material. Specimens from the following localities are believed to be true *O. lucionensis:*

Lamao, Bataan Province, and Manila, Luzon, Cuyo, Mindoro, Lubang, and Cagayancillo.

The majority of the Philippine shrikes of this genus have the under parts marked with dusky cross vermiculations, indeed it is very unusual to find an individual entirely free from these markings.

Hyloterpe winchelli Bourns & Worcester.

Twelve specimens of Winchell's thickhead.

Dicæum intermedium Bourns & Worcester.

An extensive series of this little flower pecker from Badajos. Bourns and Worcester [4] suggested the possibility that the Romblon bird might prove to be distinct from those of Tablas, but I find no points in which birds from the two islands differ; the heavier yellow wash on the throat of some of the Tablas specimens is probably due to immaturity. The young of *D. intermedium* does not differ from that of *D. sibuyanicum*, already described by me.[5]

Birds in immature plumage were taken from August 15 to September 19. The first indications of the adult plumage is a small patch of orange feathers on middle of breast. No. 10749 ♂, Bureau of Science collection, taken at Badajos, Tablas, September 5, 1905, is selected as the type of the young plumage.

Æthopyga magnifica Sharpe.

Six specimens.

Cinnyris sperata (Linn.).

An immature male, September 5.

Anthreptes chlorigaster Sharpe.

Twelve specimens taken at Badajos in August and September are in young or moulting plumage.

Anthus rufulus Vieill.

Two specimens from Tablas, August and September.

Munia jagori Martens.

One specimen.

Oriolus chinensis Linn.

A male.

Chibia menagei Bourns & Worcester. (Pl. IV.)

This very distinct species is represented by a number of skins taken in August and September. Unfortunately, the magnificent tail feathers are badly worn, this fact greatly injuring the appearance of the specimens.

Sarcops calvus (Linn.).

Ten specimens.

Lamprocorax panayensis (Scop.).

Three specimens of the Panay starling.

[4] *Occ. Pap. Minn. Ac.* 1, 18.

[5] *Publications of the Bureau of Government Laboratories*, 25, 18.

ILLUSTRATIONS.

PLATE I. *Strix candida* Tick. (young specimen).
II. Nest of *Lalage niger* (Forster).
III. Nest of *Zosterops meyeni* Bp. (with one egg).
IV. *Chibia menagei* Bourns and Worcester.
V. *Rhipidura sauli* Bourns and Worcester.
VI. *Rhipidura albiventris* Sharpe.
VII. *Rhipidura cyaniceps* (Cass).

PLATE I.

PLATE II.

PLATE III.

PLATE IV.

PLATE V.

PLATE VI.

PLATE VII.

A NEW GENUS AND SPECIES OF CULICIDÆ.

By CHARLES S. BANKS.

(*From the entomological section, Biological Laboratory, Bureau of Science.*)

Family **CULICIDÆ.**

Subfamily TOXORYNCHITINÆ.

Genus **WORCESTERIA** gen. nov.

Head with closely applied, wide, flat scales (Pl. I, fig. 1) and a very small group of upright, truncated, bastonate scales (Pl. I, fig. 2) having distal extremities crenulate, on extreme occiput, near nape; a tuft of six curved bristles projecting over eyes; thorax and abdomen with flat scales; legs and palpi with narrow flat scales. Palpi in the ♀ short, *5-jointed*, fourth and fifth almost microscopic, being, together, not as long as width of third joint, and less than ⅓ as wide as preceding joints (Pl. I, figs. 3 and 4); in the ♂ *3-jointed*, acuminate, reflexed before middle, first joint composed of three segments anchylosed and with but faint evidence of former segmentation expressed by arrangement of scales (Pl. I, figs. 5 and 6); proboscis long, tapering and curved as in *Toxorhynchites* and *Megarhinus;* distal segment bilabiate, prothoracic lobes strongly swollen, each bearing a laterally projecting, vertical row of curved spines; wing venation as in *Megarhinus*, the first submarginal cell ½ as long and ½ as wide as the second posterior, its proximal angle very acute, that of the second posterior being rather more rounded, the arrangement of the cross veins differs in the sexes, the supernumerary being farther removed from the mid cross vein in the ♂ than in the ♀ and the mid cross vein being also slightly shorter in the ♂; the cyclic vein[1] very prominent and two-parted, equally pronounced in both sexes, its curve, the reverse of that in *Megarhinus* (Pl. I, fig. 7); metanotum longitudinally slightly sulcate on median line, densely pilose; abdomen bordered laterally with sparse hairs to fifth segment, then having dense lateral tufts of variegated hairs; legs of both sexes strongly spinose except last two tarsal segments; ungues of ♀ simple and equal; those of ♂ unequal, the larger unidentate on fore and mid legs, equal on hind legs and very small; male genitalia having the bulbous basal segment strongly setose, the distal segment long, very slender, double-curved, the apical tooth being placed ventrally before the apex. (Pl. I, fig. 8.)

The type of the genus is *W. grata* sp. nov., described herewith.

I take great pleasure in dedicating this new genus in a most interesting group of insects, to Mr. Dean C. Worcester, to whose personal efforts,

[1] I have adopted this term as a name for the vein which curves upward and inward or is reflexed from the end of vein 5 into the anal cell in the *Megarhininæ* and *Toxorhynchitinæ*.

both through study and assistance, scientific research is lastingly indebted in the Philippines.

While this genus possesses characteristics of both *Megarhinus* and *Toxorhynchites,* it is so entirely different from either of them in those characters upon which these two genera are erected that I have not the slightest hesitation in placing it as distinct.

So much incertitude has existed in the matter of palpal segmentation that it is most gratifying to have been able to breed and study a large series of individuals and by that means to have been able, by careful dissections, to found the genus upon certainties. I fear that inability to obtain large numbers of individuals in this as in other subfamilies, has been the source of no little confusion as to important features.

I personally do not approve of one-species genera and should have preferred studying species in the other genera of this subfamily before forming this one, but I am certain that when such study is made other species now supposed to belong to *Megarhinus* and *Toxorhynchites* will fall here.

Worcesteria grata gen. et sp. nov.

Length ♂ 12 millimeters, proboscis 7 millimeters, ♀ 10 millimeters, proboscis 7 millimeters, length of wing 8.25–8.75 millimeters; head, thorax and abdomen dark, metallic brownish-blue, the head and mesothorax being lighter blue laterally as are the prothoracic lobes and the dorsal ridge of the first abdominal segment. Legs variegated blue, wine-color and orange-yellow, the last color in the ♀ only, the leg bands being different in the sexes and containing much white in the ♀.

♀, head with flat, light-greenish variegated metallic scales, a few dark, crenulately truncated, bastonate scales on extreme occiput near nape (Pl. I, fig. 2); region of eyes with lighter scales; 6 long, brown, curved bristles projecting over the eyes which are dark-wine-color or bronze in certain lights; antennæ sparsely setose, the setæ on each segment not more than 5 in number, being placed externally at the base of each; first segment covered basally with dark-green, apically with white scales, second segment swollen basally, 1½ length of succeeding segments and having a dorso-internal tuft of greenish-brown scales on basal half only; other segments with dense, gray pile; palpi ¼ length of proboscis, *5-jointed* (Pl. I, fig. 3), first segment as long as wide; second, about four times length of first; third, nearly twice length of second; fourth and fifth, extremely small, their combined length being less than width of third and their width being less than ⅓ that of antepenultimate. The apex of the third segment is concave *not rounded,* and receives the fourth to half its length (Pl. I, fig. 4); scales of palpi dark-purple, disposed in 2 groups giving the appearance of but 2 segments, the distal portion of each group is of white scales, those at the apex completely covering the fourth and fifth segments; third segment strongly laterally and apically spinose, there being 3 large spines at extreme apex extending beyond fifth segment (not shown in fig. 4). Fourth segment bears a single strong spine. The denuded palpus is moderately pilose (Pl. I, fig. 4), proboscis ⅔ length of body, when latter is normal (not shrunken), dark-purple or wine-color, with strong iridescence; the distal segment bilabiate with sensitively setose apex.

Prothoracic lobes strongly swollen, occupying angle between head and mesonotum, covered with scales of same color as those on head and with a vertical row of laterally projecting bristles; pronotum with dark-green, narrow, flat scales grading to very light-green laterally and cupreous on posterior margin; a single,

irregular patch of pure-white scales covers the pluræ; chetæ as follows: a downward and backward projecting group of brown bristles at middle of side of pronotum, a group of golden brown over root of wing, and an ill-defined group scattered between these two; scutellum with light-green, flat scales as on sides of pronotum and a marginal row of golden bristles; metanotum very dark-brown, longitudinally slightly sulcate on median line, and densely pilose.

Abdomen with green scales dorsally on basal segments, purplish or wine-colored on apical, first segment nearly all white, save a dorsal green patch; second and third, green with lateral white patch; fourth, nearly all green with faint suggestion of white laterally; fifth, as third but with some purplish scales and small white tuft; sixth and seventh, purplish, the former having lateral tufts of white and yellow, the latter, tufts of dark-brown; eighth segment, subtriangular, with green scales and yellow lateral tufts; venter, with purplish or violet-brown scales, the white patches of the dorsum being almost duplicated below, except on sixth segment, which is as fifth.

Legs variegated and banded; coxæ with large lateral patches of pure white scales, femora with dark-green and white areas, the anterior being all green, the middle internally whitish basally, the posterior, externally for nearly whole length; anterior tibiæ bluish-green externally with narrow, yellow stripe internally; mid tibiæ golden-yellow except at apex which is dark-blue-green and a mottled area externally at base, posterior tibiæ all dark-blue-green except a narrow, internal area in its middle; anterior metatarsi pure white with green at base; mid metatarsi the same, minus the blue-green at base, only a faint suggestion of which is left; posterior all dark-blue with white, mottled area over their basal third; anterior tarsi purplish-brown-green except first, which is white for nearly its whole length, then brown; mid tarsi white, except last segment which is brown-green; posterior tarsi same as anterior; ungues on all legs simple and of about same size.

Wings fuliginous, and irridescent, the veins having bluish-purple scales; first submarginal $\frac{1}{2}$ length and $\frac{1}{2}$ width of second posterior cell, its proximal angle very acute, that of the second posterior rounded; mid cross vein nearer base of wing than posterior. (Pl. I, fig. 10.) The cyclic vein very strongly developed and curving from end of vein 5 upward and inward in first anal cell, its branch curving downward and outward being partially parallel with wing margin. (Pl. I, fig. 7.) Halteres basally swollen, pale-yellow; knobs lighter, with few dark scales.

♂ similar in general coloring to ♀ except as follows: Scutellar bristles dark-brown, abdomen dorsally, dark-green basally to dark-purplish-blue apically, second to fifth segments having only faint suggestion of white laterodorsally; anal tufts black in all segments except eighth which has a few golden bristles, more evident ventrally. Ventrum with white, lateral patches on fifth and sixth segments, occupying a total of $\frac{2}{3}$ their width; on other segments a slight indication of these patches in form of a light line. Legs, with dark-blue-green scales on all segments, a white longitudinal area on the posterior femora externally and internally. The mid and posterior metatarsi and first tarsal joints have light-green bands basally, otherwise all dark-blue-green. All legs in ♂ and ♀ strongly spinose with exception of tarsal segments.

The eyes of the ♂ are blue-black; the antennæ have first joints black, with white pruinescence, the second twice as long and 1.5 times as wide as any succeeding; all joints except last 2 with fine, brown pubescence and whorls of long, dense, brown bristles at their middle; last 2 joints filiform and setose with whorls of bristles from their bases; clypeus black with white pruinescence, its margin bicrenate; palpi very long, $\frac{3}{4}$ length of body and slightly longer than proboscis, reflexed at their middle, *3-jointed* (Pl. I, fig. 5) and strongly scaled, the

arrangement of the scales giving the appearance of 2 extra joints (Pl. I, fig. 6), the first segment composed of 3 anchylosed segments; general color, dark-blue-green with scattered light-green scales on dorsal aspect; distal segment, strongly acuminate and spined, as are the two preceding, at their apices only. Venation of wings as in ♀ except that mid cross vein and posterior cross vein are contiguous; supernumerary is farther removed from mid cross vein than in ♀. (See Pl. I, figs. 9 and 10 for arrangement of cross veins.) The posterior cross vein appears to be unstable in its position, varying in ♂ and ♀ in specimens other than the types, but the same relative position of the 3 veins is maintained in the sexes. Halteres basally swollen, ochraceous; knobs lighter with few dark hairs. Genitalia having basal segment bulbous and strongly spinose-setose, the distal segment long, slender, double-curved, the apical tooth being placed ventrally before apex. (Pl. I, fig. 8.) Length of ♂ 12–13 millimeters; length of wing 8.25–8.75 millimeters; length of palpi 7–7.5 millimeters.

Negros Occidental, P. I., Bago, Hacienda "Louisiana," Mailum, alt., 150 meters; and Cebu, P. I., Cebu. (*Banks, McGregor, Coll.*)

Time of flight, June, July; adults from bred specimens, 24 June, 1906.

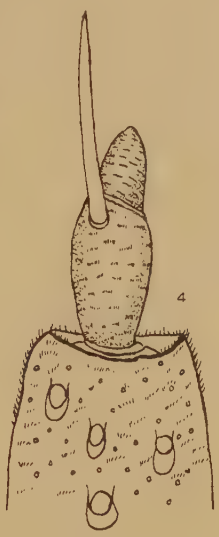
Types of ♂ and ♀, No. 6071 in Entomological Collection, Bureau of Science, Manila, P. I. There are 18 cotypes in the collection.

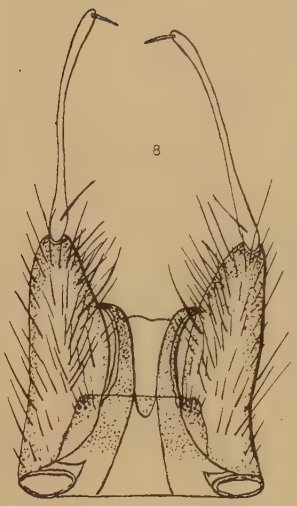
The name of this species is suggestive of the fact that aside from its beautiful appearance, it not only *does not bite,* but its larvæ destroy enormous numbers of noxious forms of *Culicidæ,* having fed most willingly upon those of *Culex fatigans* Wied., *Stegomyia scutellaris* Walk., var. *samarensis* Ludl., and *S. fasciata* Fabr., *var. nov.,* in the laboratory and in their natural habitat, upon those of at least two other, as yet unidentified, species, one of which is probably *Desvoidya* sp. This insect has been reared and is very easy to breed. A full description of its life history and habits will soon be published.

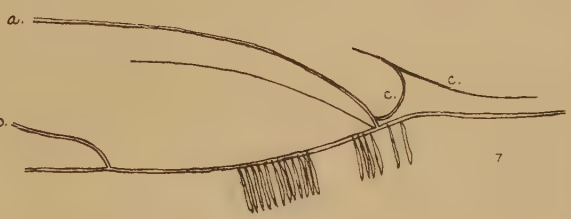
ILLUSTRATIONS.

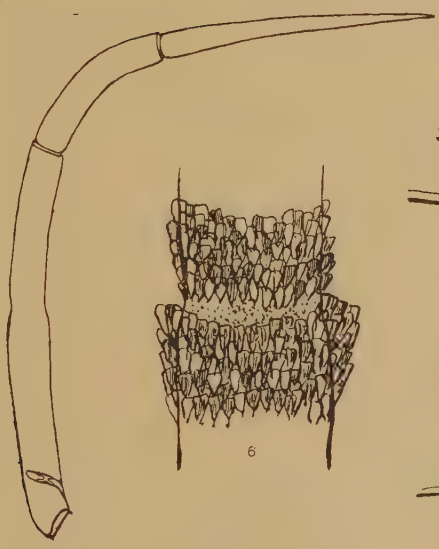
PLATE I.

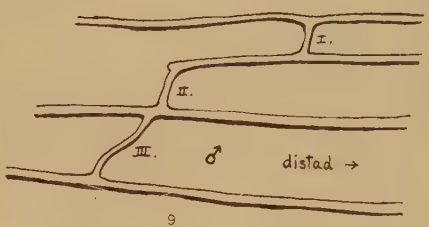
FIG. 1. *Worcesteria grata* gen. et sp. nov., typical scale from occiput. × 400.
2. Bastonate scale. × 400.
3. Palpus of female. × 45.
4. Same showing apex of third segment and fourth and fifth segments. × 200.
5. Palpus of male showing mid-stricture of first segment and remains of anchylosed joint near base of same. × 15.
6. Palpus at middle of its first segment showing stricture and arrangement of scales to give appearance of articulation. The same scale arrangement is found at base of first segment. × 105.
7. Margin of wing showing position of cyclic vein. × 45.
   a. Fifth longitudinal vein.
   b. Sixth longitudinal vein.
   c. Cyclic vein, with its branching.
8. Male genitalia showing basal and distal segments, the latter bearing apical ventral spines, and the harpes shown between basal segments as two outward curving hooks. × 50.
9. Arrangement of supernumerary and cross veins in male. × 45.
   I. Supernumerary.
   II. Mid cross vein.
   III. Posterior cross vein.
10. The same of the female. The arrows in each case point toward apex of wing. × 45.











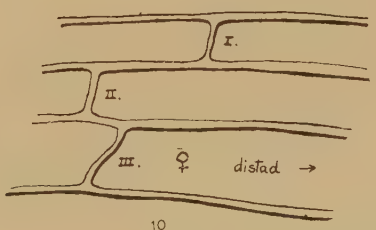


PLATE I.

A CHANGE OF NAME IN COCCIDÆ.

By Charles S. Banks.

Since the publication of descriptions of certain new species of *Coccidæ* in The Philippine Journal of Science (1906), **I**, 230 *et seq.*, my attention has been called to the fact that *Chionaspis candida* had already previously been used by Green in the description of a species from Australia.[1]

In consequence of this previous use of the name *candida*, I propose to change the name of my species to *Chionaspis inday*[2] Banks in place of *Chionaspis candida* Banks as given on page 232 of The Philippine Journal of Science and also on page 222 of the Journal in Part II of "The Principal Insects Attacking the Coconut Palm."

[1] *Victorian Naturalist* (1905), **22**, 6.

[2] Inday (pron. *in-die*): A Visayan term meaning "little one."

REVIEWS.

The World's Anatomists: Concise Biographies of Anatomic Masters, from 300 B. C. to the Present Time, Whose Names Have Adorned the Literature of the Medical Profession. By G. W. H. Kemper, M. D., Professor of the History of Medicine in the Medical College of Indiana. Revised and enlarged. Paper; 11 illustrations, 9 of which are portraits. Pp., xiv + 79. Price, $0.50. Philadelphia: P. Blakiston's Son & Co., 1905.

This small book will find a place on the table of the anatomist or of the general scientific worker in biological subjects, as a concise tabulation of the names and of a few important facts in the careers of a number who have worked in the field of anatomy.

It will also serve to assist somewhat in the study of nomenclature. For the student of the history of medicine it will be of but little value, as it is a tabulation and not a discussion from the historical standpoint.

Treatise on Diseases of the Skin for the Use of Advanced Students and Practitioners. By Henry W. Stelwagon, M. D., Ph. D. Fourth edition, thoroughly revised. Cloth; 258 illustrations in the text and 32 full-page lithographic and half-tone plates. Pp., 1136. Philadelphia: W. B. Saunders & Co., 1905.

Stelwagon's Treatise on Diseases of the Skin would appear peculiarly adapted to the use of the general practitioner by reason of the clear and concise manner in which the various affections are described. A happy faculty of paragraphing, and in this way of presenting separately the important questions to be considered in understanding a disease, gives one a comprehensive grasp of the disease entity which is not always obtained in works on skin.

The fourth edition of this excellent work is filled with plates and illustrations which greatly assist one who is not a specialist in this branch of medicine and the lack of which makes certain other similar volumns less well adapted to the use of the man in general practice.

The paragraphs on diagnosis, under the heads of psoriasis and eczema, impress one as most clearly expressed, and the entire article on eczema is clear and to the point. The discussion of tuberculosis of the skin and that of syphilis are of great practical value, and many of the illustrations under these subjects are more instructive than columns of written matter would be. The affections due to parasitic yeasts and molds are briefly but well presented, the article on blastomycetic dermatitis being particularly satisfactory.

However, many of the diseases in which those working in the Tropics are peculiarly interested receive little more than brief mention. Thus, under the discussion of Delhi boil, or tropical ulcer, there is not even a reference to the work of the various recent investigators of the etiology of these widespread affections, no mention being made of the work of Wright, Strong, or James.

Dhobie itch, the skin affection which in so many of the tropical countries peculiarly impresses its characteristics upon the tourist, is described in a general and rather misleading way.

After all is considered, it is necessary to admit that it would be difficult to conceive of a work more to be recommended for the purpose designated in the preface, namely, as a guide for those engaged in general practice.

E. R. S.